The Pennsylvania State University

The Graduate School

Graduate Program in Kinesiology

SUBMAXIMAL CYCLE ERGOMETRY AS A PREDICTOR OF MAXIMAL AEROBIC CAPACITY IN WOMEN ON ORAL CONTRACEPTIVES

A Thesis in

Kinesiology

by

Jannell C. MacAulay

Submitted in Partial Fulfillment
of the Requirements
for the Degree of

Master of Science

December 1999

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	17.Sep.99	THESIS

4. TITLE AND SUBTITLE

SUBMAXIMAL CYCLE ERGOMETRY AS A PREDICTOR OF MAXIMAL AEROBIC CAPACIATY IN WOMEN ON ORAL CONTRACEPTIVES

5. FUNDING NUMBERS

6. AUTHOR(S)

2D LT MACAULAY JANNELL C

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

PENNSLYVANIA STATE UNIVERSITY

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

THE DEPARTMENT OF THE AIR FORCE
AFIT/CIA, BLDG 125
2950 P STREET
WPAFB OH 45433

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

FY99-304

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION AVAILABILITY STATEMENT

Unlimited distribution
In Accordance With AFI 35-205/AFIT Sup 1

12b. DISTRIBUTION CODE

DISTRIBUTION STATEMENT A
Approved for Public Release
Distribution Unlimited

13. ABSTRACT *(Maximum 200 words)*

14. SUBJECT TERMS	15. NUMBER OF PAGES
	84
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT

Jannell C MacAulay

Jannell C. MacAulay

We approve the thesis of Jannell C. MacAulay.

Date of Signature

Joseph G. Cannon
Professor of Physiology and Kinesiology
Kinesiology Graduate Program Director
Thesis Advisor

8/9/99

W. Larry Kenney
Professor of Physiology and Kinesiology

8/9/99

Nancy I. Williams
Assistant Professor of Kinesiology

8/9/99

ABSTRACT

Predicted maximal aerobic capacity (VO_2max), using submaximal exercise tests, is used to evaluate fitness for job performance, especially within the military. Women who use oral contraceptives experience a rhythmic variation of circulating synthetic hormones that can influence submaximal exercising heart rate. The purpose of this study was to examine the validity and reliability of two submaximal heart rate-dependent cycle ergometry exercise tests, one used by the Air Force (AF) and one suggested by the American College of Sports Medicine (ACSM), for women using oral contraceptives. Eighteen healthy and fairly active women, aged 19-22 years, completed a maximal treadmill exercise test with indirect calorimetric determination of VO_2max followed two days later by submaximal testing. Each of the three tests were conducted in both the quasi-luteal (Q-L) phase (the second week of the active pill) and the quasi-follicular (Q-F) phase (the last 3 days of placebo administration). VO_2max was lower (by 1.1 ± 0.63 ml/kg/min) in Q-L than in Q-F (Q-L = 38.2 ± 1.1 ml/kg/min, Q-F = 39.3 ± 1.1 ml/kg/min, $P = 0.055$). Comparison of VO_2max predicted by the AF test to the true maximal value revealed a slight, statistically non-significant (1.5%) overestimation in the Q-L phase (AF = 38.8 ± 1.8 ml/kg/min vs Max = 38.2 ± 1.1 ml/kg/min, $P = 0.3$) and a larger underestimation (5%) in the Q-F phase (AF = 37.4 ± 1.8 ml/kg/min vs Max = 39.3 ± 1.1 ml/kg/min, $P = 0.06$). Between the two phases, the predicted values of the AF test were significantly different (Q-L = 38.8 ± 1.8 ml/kg/min, Q-F = 37.4 ± 1.8 ml/kg/min, $P = 0.02$). The ACSM test underestimated VO_2max in the Q-L (3%) phase and significantly

underestimated in the Q-F (8%) phase (Q-F = 36.1 ± 1.4 ml/kg/min vs Max = 39.3 ± 1.1 ml/kg/min, $P = 0.003$). Heart rates were significantly higher ($P = 0.02$) in the Q-F phase as compared to the Q-L phase. A prospective ACSM equation for estimating maximal aerobic capacity, to be published in the 6th edition of *ACSM's Guidelines for Exercise Testing and Prescription*, was also evaluated. The newer ACSM equation provided a slightly better estimate than the original ACSM equation in both the Q-L (2.4% underestimation) and Q-F phases (7.3% underestimation). Deviations between predicted and true maximal values were independent of fitness level, body weight changes between phases and pill formulations. The AF and ACSM (using the new equation) heart rate-based submaximal cycle ergometry tests are valid (within 5% of the measured value) predictors of maximal aerobic capacity in women on oral contraceptives in the Q-L phase. However, neither test provided a reliable measurement between the two phases. The significant heart rate differences between the two phases were the cause of the differing estimations of VO_2max that were closer to measured values in the Q-L phase.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ACKNOWLEDGMENTS

First of all I would like to express my thanks and sincere appreciation to my thesis advisor, Dr. Joe Cannon. When most thought it was impossible to complete a thesis and the necessary graduate credits for a master's degree in one year, Joe accepted me as a student. He guided me into thinking independently and designing a project that we both could be proud of. He had complete confidence in my ability to successfully complete my requirements and always pushed me to my fullest potential. I think he got a little more than he bargained for by accepting both me and Brittney as graduate students and I thank him for being patient with us.

I would also like to thank the other members of my thesis committee: Dr. W. Larry Kenney and Dr. Nancy Williams for their patience, encouragement and guidance during the course of this study. They never hesitated to share their knowledge and advice whenever I had a question or frustration.

I am forever indebted to my partner and friend, Brittney Salkeld. How was I to know that I would meet an individual that would touch my life with such power in the short time I was at Penn State? I am so thankful that Brittney and I ended up here to make it through our graduate programs together. We have always said that God brought us here for a reason: to accomplish our goals and to make a lifelong friend. She was a source of inspiration and companionship during the months of preparation, testing and

writing. Together, with laughter and fun, we developed our own unique way of conquering graduate school. I truly could not have done it without her!

Thank you to Jan, Lori, Paula, Dr. Ann Trout and the rest of the GCRC staff for putting up with the scheduling conflicts, dealing with the blood draws and their tolerance of our unique approach to science. Their invaluable assistance helped us to finish our testing on time. Thank you also to my subjects, who not only shared their wisdom of undergraduate civilian college life but also showed up at 7 AM or in between classes on four separate occasions to perform the tests for this study.

Thank you to Rick Ball for his patience during the course of this year. He allowed Brittney and I to invade his office space and turn his workday upside down with our obnoxious laughter, crazy stories and wedding talk. He also shared his knowledge of laboratory techniques, as well as his lab with us during the three months of sorting through urine and blood. I am grateful to him for tolerating a fun and enjoyable office and laboratory atmosphere because I don't think I would have finished without it!

I would like to thank the United States Air Force for this amazing opportunity. Although I was only able to spend one year at Penn State, I am grateful that I had the wonderful opportunity to study a subject of my interest at a civilian institution. Also, to Pete Flatten at Brooks AFB and Major Patrick Bradshaw who helped me to aim my study towards "real Air Force" applications. Major Bradshaw supported me from the beginning by helping me get to Penn State when it seemed impossible and by helping me

set time tables and goals for myself. Pete was always there to answer any questions or help with the computer program that seemed to have a mind of its own!

Finally, I am extremely thankful to my husband Chris for all of his love and support during this very hectic but rewarding year. I would not have accomplished this task without his confidence and faith in my abilities and his patience during the times of frustration. Even though we were miles apart I felt his presence in my heart, motivating me along the way. I am also thankful to my family, especially my parents who have always encouraged me to succeed through their love, support and faith. Most importantly, I would like to thank God for all of the wonderful blessings, gifts and opportunities he has given me. I have accomplished something I never thought possible and I am forever grateful to those who gave me the strength to accept the challenge and succeed.

Chapter 1

INTRODUCTION

Maximal oxygen uptake, or aerobic capacity, is used to determine an individual's physiological fitness level. Aerobic capacity is dependent upon the ability of the cardiovascular system to transport oxygen from the atmosphere to working muscles and the ability, at the cellular level, to use the oxygen for energy production (24).

The maximal rate of oxygen consumption (VO_2max) is the most commonly used measurement of an individual's aerobic capacity. VO_2max is measured using laboratory techniques involving maximal treadmill or cycle ergometer exercise which requires sophisticated equipment, a large time commitment and a great deal of expertise (40). There are also potential risks and complications associated with testing older adults or individuals with conditions such as asymptomatic coronary heart disease (4, 24). It is unrealistic to suggest that VO_2max be measured directly for entire populations or by individuals who do not have laboratory facilities readily available to them. The United States Air Force, for example, could not subject all of its members to such a complex and expensive test for the purpose of fitness screening. This necessitates submaximal tests that provide an estimate of VO_2max. Physiologists have developed several different submaximal tests to estimate VO_2max that are based on a linear relationship between heart rate response and VO_2 or workload (43). These include treadmill walking, cycle

ergometry and platform stepping (24). Submaximal cycle ergometry is the most popular method used to estimate maximal aerobic capacity, however results vary in validity and reliability.

In the last decade, there has been a three-fold increase in the number of women participating in jobs that require high levels of fitness within the armed forces. Using VO_2max values as an indicator of cardiovascular health, and thus fitness level, is common. The Air Force developed a submaximal cycle ergometry test to avoid the issues associated with a maximal test described above. The low risk, submaximal test must be a valid predictor of aerobic capacity if the result is to be used to identify an individual at a certain fitness level. Accurate predictions of female VO_2max are necessary when the concern is meeting minimal physical standards for employment or job placement, especially within the military (24, 32, 70).

Female-specific factors such as the menstrual cycle and the use of oral contraceptives are not accounted for during submaximal testing. Previous research shows that the female menstrual cycle does not appear to limit maximal exercise performance in women (13, 22, 35, 42) and has minimal effects on submaximal exercise (6, 13, 27, 28). The influence of oral contraceptives on maximal and submaximal exercise performance is more controversial (6, 22, 36, 42, 54). However, these factors have not been studied in regard to the reliability and validity of submaximal testing.

Female military personnel are prescribed oral contraceptives (OC) for a wide range of purposes, including contraception, menstrual regularity and control of premenstrual symptoms. The Air Force submaximal cycle ergometry test does not take this variable into account during its personnel testing. Many OC contain a combination

of synthetic estrogens and progestins, and some formulations contain synthetic progestins only (36). Studies suggest that the synthetic hormones are more potent than their endogenous counterparts in preventing ovulation and inducing endometrial proliferation (64) however, their influences on physiological responses during exercise are not well established. The complex hormonal changes occurring during female reproductive life, during both ovulatory and OC pill-controlled cycles, have not been extensively studied in regards to their effect on exercising women.

Female reproductive cycles involve a rhythmic variation of either endogenous hormones (found in the normal menstrual cycle) or exogenous hormones (found in the oral contraceptive pill) (36). During exercise, these hormones will influence heart rate which is the basis for the submaximal cycle ergometry tests. The potential exists for changes to occur in submaximal predictions of maximal aerobic capacity due to the altered heart rate, caused by the fluctuating hormones, particularly the exogenous ones (6, 10, 22, 23, 26, 42, 52, 54, 62). The administration of submaximal tests in the different phases of the female reproductive cycle, particularly for those women on oral contraceptives, may lead to variable results. Reliability tests need to be conducted to determine whether submaximal cycle ergometry can be used as a valid and reliable estimate of maximal aerobic capacity, throughout a cycle in women using oral contraceptives.

Hypothesis

This project tested the hypothesis that submaximal cycle ergometry tests (the Air Force test and the American College of Sports Medicine (ACSM) test), based on a linear heart rate-VO_2 relationship, greatly underpredict the aerobic capacity of women using oral contraceptives during the quasi-luteal phase of their menstrual cycle. This hypothesis was based on the following observations: Endogenous progesterone has been known to increase basal body temperature and the heart rate response to exercise in some women (23, 26, 52). Women using oral contraceptives ingest synthetic hormones that also cause alterations in submaximal exercising heart rate. These differences, in turn, could confound results in submaximal tests that are based on a linear heart rate-VO_2 relationship. Previous research has revealed conflicting results in regard to heart rate response during submaximal exercise testing in women on OC. Heart rates have increased by 6-7 beats/min for women while taking oral contraceptives compared to when they were taking a placebo (54), heart rates have remained unchanged between phases (9, 22, 42), and heart rates have decreased from testing in the luteal phase of a normal cycle to the corresponding quasi-luteal (Q-L) phase following the administration of OC (23). Charkoudian and Johnson measured heart rate differences in women on OC during whole body heating and found higher heart rates in the placebo phase (10) and Lebrun et al studied the differences in maximal heart rates during exercise in a normal environment and found no significance (36). There are many different types of OC on the market and different combinations were used in the previously mentioned studies, which could be one reason for the dissimilar results. Due to conflicting findings more

research is needed regarding the influence of each synthetic hormone, in the various OC formulations, on heart rate during exercise testing.

This study analyzed both the AF and ACSM cycle ergometry tests. The AF test is based on the Astrand-Rhyming (A-R) nomogram for calculating aerobic capacity from heart rate response to submaximal work (4). Since the origination of the nomogram there have been several validation tests and modifications for age and initial workload (3, 57). The actual AF test, although based on this nomogram and subsequent modifications, uses a computer program to determine the estimated VO_2 max. During the test, the subject works at a predetermined workload based on age, sex, weight, and exercise history. The subject pedals at a set rate for a given amount of time (6 minutes), where a steady state heart rate (between 125-170 beats/min) can be reached. The heart rate response to this work determines the individual subject's estimated aerobic capacity through the use of the computer calculation that is based on the A-R nomogram.

The ACSM test relies on the linear relationship between heart rate and workload, however, not the heart rate response to a single workload like the AF test. An individual's maximum exercise intensity is computed by extrapolating submaximal heart rate response to progressive increases in workload to the age-predicted maximum heart rate. This maximum exercise intensity value can then be entered into the ACSM equation and a VO_2max value can be estimated (43).

Several studies have questioned the reliability of submaximal testing for both men and women. There has been a consistent underprediction in males with the validity of the underpredictions, when compared to measured VO_2max values, varying from 15-30% (4, 12, 40, 50, 55, 69). Submaximal testing of women has resulted in overpredictions that

range from 3-21% depending on the mode of the maximal exercise test (cycle ergometer vs. treadmill) (24, 57, 71) and underpredictions up to 15% (12, 40, 50). Not one of these studies took the menstrual cycle or oral contraceptives into account during exercise testing.

Specific Aims

The specific aims of this study were to analyze the validity and reliability of two submaximal, heart rate-dependent cycle ergometry tests as predictors of VO_2max in women on oral contraceptives; the Air Force modified A-R protocol and the ACSM submaximal test protocol. Values within ± 5% of actual measured VO_2 max were considered valid and reliability was determined by the consistency between the two measurements in each phase of the cycle. This study also assessed the effect of oral contraceptives, particularly progesterone-like synthetics, on heart rate during submaximal exercise.

Chapter 2

REVIEW OF LITERATURE

A-R Submaximal Cycle Ergometry

The United States Air Force has adopted a submaximal cycle ergometry test as an estimate of aerobic capacity, or maximal oxygen uptake (VO_2max), to determine the fitness levels of its military members. This is important for force readiness during times of crisis. Maximal oxygen uptake is dependent upon the capacity of the cardiovascular system to transport oxygen to working muscles and the ability, at the molecular level, to use the oxygen effectively. This value can be measured and estimated through the use of submaximal exercise tests that measure heart rate responses to steady-state exercise. In 1954, Astrand and Rhyming developed a nomogram for predicting aerobic capacity from heart rate responses to submaximal workloads in cycle or step test exercise (4). The test was based on the attainment of a steady-state heart rate of 125-170 beats/min during the last 3 minutes of the 6-minute test (25). The original validation group consisted of 58 well-trained male and female subjects between the ages of 18 and 30. In 1960 the nomogram was revised to add an age correction factor and to account for the differences in mechanical efficiency at lower workloads and in VO_2 at a given workload between men and women (25). However, once again after further validation studies, it was later modified to a lower initial exercise rate and shorter duration (57). The Air Force, along

with Dr. Loren Myhre of the Human Systems Division, has since adjusted the test for use with Air Force personnel (69). Dr. Myrhe developed a computer program that included specific criteria for determining the initial workload and for increasing the workload during the early minutes of the test (47). This was done in order to increase the subject's heart rate to the desired steady states during the last minutes of the test (46). During the test, the subject pedals at a set rate against a predetermined resistance (based on age, sex, weight and exercise history) for a given amount of time. Measuring the efficiency of the subject's heart-lung-muscle "machine" is estimated by heart rate increase as a result of the workload (60). Using the computer program based on the Astrand-Rhyming (A-R) nomogram and its modifications, an estimated VO_2max for the subject can be calculated. The computer program uses a computation containing age, weight, height, average ending heart rate, a conversion constant for body surface area and final workload to determine the estimated aerobic capacity. It should be noted that the AF test protocol uses a constant power load, maintained for 6 consecutive minutes, in which a steady-state heart rate between 125 and 170 beats/min is reached (40). It is at this steady state that heart rate and power load are used to estimate VO_2 max (4). This estimation is then used by the AF to determine a fitness standard based on the 1995 ACSM percentiles (see Table 1) (43).

Fitness Category	ACSM Percentile	<30 years	30-39	40-49	50-59	60+
Superior	>75th	>39.54	>37.38	>35.12	>39.91	>30.88
Good	51st-75th	35.21-39.53	33.77-37.37	30.88-35.11	28.23-39.90	25.83-30.87
Fair	26th-50th	30.95-35.20	29.94-33.76	27.99-30.87	25.10-28.22	23.66-25.82
Poor	<25th	<30.94	<29.93	<27.98	<25.09	<23.65

Table 1. Women's Fitness Standards for Cycle Ergometry (VO_2 Values)

Since a substandard fitness rating will require an individual to be put on a strict fitness program and a probationary fitness status, and a higher rating could be a false indicator of proper physical readiness, it is important that results are accurate. In general the A-R test results in reasonable, but not always valid, estimates of VO_2 max. In males, A-R submaximal cycle ergometry tests have been known to underpredict O_2 uptake values by 17-20% (25, 69). Williford et al also found that due to the underpredictions of VO_2 max, out of the 50 officers tested, 68% were placed 1-2 fitness categories below where their actual levels placed them (69). Hartung et al found that although the A-R test underestimated VO_2 max values by 20%, it was consistent in overpredicting high fit individuals and underpredicting low fit individuals (25). However when Rowell et al measured the predictive ability of the A-R equation in trained and untrained subjects they didn't see an overprediction in the trained subjects. They found a 6% underestimation in trained individuals and a 26.5% underestimation in untrained subjects that became a 14% underestimation after training (55). Other studies demonstrated that males were underpredicted by 5-25% compared to either treadmill or cycle ergometer maximal tests (12, 50, 55, 69). In women, the A-R cycle ergometry test tended to overestimate VO_2max by 8.5% compared to the treadmill maximal values and 18.5% compared to the

cycle maximal values (24, 71). Other studies using the A-R protocol have overpredicted VO_2max by up to 21% in women (24, 57, 58, 71). Patton et al, when studying the validity of the A-R test in 15 men and 12 women found the overall underestimation for both sexes to be 16.2% (50). While Davies et al found a 15% underestimation in the same test for both men and women (12). Finally, a study using 35 women and 15 men, found that the A-R based AF submaximal cycle ergometery test underpredicted maximal VO_2 values by approximately 15% (40). In women, a wide range of estimates for the prediction of VO_2 max, both underpredicting and overpredicting, exist (See Table 2). It is worthwhile to note that none of these studies looked at the female menstrual cycle as a variable.

Reference	Age/Sex/# of Participants	Variables Measured	Tests Evaluated	Results
Astrand and Rhyming (1954)	58 well-trained males and females (age 18-30)	HR, VO_2, Body weight and workload- No regard to MC	Max test, step test, CE test, TM test	Found nomogram: M: underpredict 8% F: overpredict 10%
Rowell et al. (1964)	113 trained (T) and untrained (UT) males & females	HR and A-R test before and after training	A-R submaximal cycle ergometry, max TM test	Underprediction of 6% in T and 26.5% in UT- turned to 14% underprediction after trng
Davies et al. (1968)	80 males and 30 females	Validity of A-R CE test, HR at various stages-	A-R CE test, max TM test	15% undeprediction in both M and F
Patton et al. (1968)	15 males and 12 females	Validity of A-R CE test	A-R CE test, max TM test	16% underprediction for both M and F
Siconolfi et al. (1982)	50 inactive males and females (age 20-70)	Validated A-R eqn	A-R CE test protocol, Max CE test	9-13% overpred. M, 20% overpred. F- altered protocol by lowering initial WL
Siconolfi et al. (1985)	Females	Validating A-R eqn with 2 tests	A-R CE test and step test, Max CE	3% overpred. F
Zwiren et al. (1991)	38 females (~ 33 years)	Compare max values on TM and CE to 5 SM tests	TM/CE max test, 2 SM CE tests, run, walk and step	A-R overpred. 8.5% for TM and 20% for CE
Hartung et al. (1993)	22 male- 11 fit, 11 unfit (age 26-45)	Validated A-R eqn	A-R CE test and max TM	20% underprediction
Williford et al. (1994)	50 male AF officers	Validity of AF CE test	AF CE test, max TM test	17% underprediction
Hartung et al. (1995)	37 women (age 19-47)	Reliability and validity of A-R CE	AF CE test vs. max TM and max CE	8.5% overpred. for TM, 18.5% overpred for CE
Lockwood et al. (1997)	15 males and 35 females (age 20-55)	Validity of AF test and PROG test No regard to	Max TM, 3 AF CE tests, one PROG test	15% underprediction for AF test

Table 2. Varying Reliability in both Men and Women in regard to Submaximal Cycle Ergometry

The A-R test has been compared to various other attempts at deriving a "better" method of prediction, based on the same premise that heart rate and VO_2 are linearly related. Maritz et al designed their own prediction method based on the extrapolation of VO_2max from the regression line calculated from HR and VO_2 at four different workloads (45). However, it was later found by Rowell et al that the Maritz et al

extrapolation method was no better than the A-R prediction method (55). Fox et al developed a submaximal cycle ergometry equation based on the results of untrained college-aged males, which like the A-R equation used heart rate response to a single workload for predicting VO_2max (18). Margaria and associates developed a similar prediction method to the A-R test using submaximal stepping workloads (44). Lockwood et al compared the A-R method to a progressive cycle ergometry test that used an incremental 8-minute protocol separated into four 2-minute stages. The estimated VO_2max value, which was calculated based on the relationship between workload and O_2 uptake and the linear relationship between heart rate and work rate, provided a valid estimate. Yet only 23% of the subjects had an estimated VO_2max that was within ± 5% of their true max value (40). Most of these competing prediction methods have found little success in surpassing the familiarity and reasonable accuracy of the A-R test during their own validation studies. The A-R protocol remains perhaps the most commonly used standardized submaximal test that provides an estimation of VO_2max.

ACSM Submaximal Cycle Ergometry

Today, many corporations are using submaximal tests in employee health care programs (21). Once again, no matter the submaximal testing method, test validity is imperative if the test will provide information concerning fitness levels of employees. Therefore in order to offer an alternative to the A-R based AF cycle ergometry test a different submaximal cycle ergometry test used for fitness testing was evaluated. Another submaximal test is the American College of Sports Medicine (ACSM) cycle

ergometry test, based on the linear relationship between heart rate and workload. The testing protocol involved a workload progression of four stages. The subject's heart rate needed to stabilize and reach a steady-state prior to the increase in workload for the next stage. The heart rate response obtained from the four submaximal exercise intensities was extrapolated to age-predicted maximal heart rate. The maximal exercise intensity was found by dropping a vertical line from the maximal heart rate to the intensity scale. This estimated maximal exercise intensity was then used to calculate the predicted VO_2max (43). According to the ACSM equation, the maximal exercise intensity is related to VO_2 in the following:

$$VO_2\ (\text{ml/min}) = 3.5\text{ml/kg}\cdot\text{min} \times \text{kg body weight} + 2.0 \times \text{power output (kgm/min)}$$

Similar to the A-R prediction method, the ACSM protocol and equation have been revised and modified several times. In 1991, the ACSM published the fourth edition of its guidelines that included a modification to the protocol and equation of the ACSM extrapolation method for the prediction of VO_2max (1). The testing protocol involved four 2-minute stages of progressive increases in workload, with cessation of the test if the individual reached 65-70% of their age-predicted maximum heart rate (1). In 1992, Lang et al found that this ACSM cycle ergometry test underestimated actual VO_2 values at all four workloads from 9-58% and subsequently designed a new equation (33). Following this, other researchers found the ACSM equation to be inaccurate and also designed their own new equations (5, 34). Anderson and Wadden attempted to find the validity of both the ACSM equation and the revised Lang et al equation for obese women

ages 23-60 (2). They found that the ACSM equation underestimated VO_2 at all workloads while the Lang et al equation provided a better estimate (2). In a study by Greiwe et al, the ACSM submaximal protocol was analyzed for reliability and validity in 15 men and 15 women aged 21-54. Each subject completed a maximal cycle ergometer exercise test, followed by two submaximal ACSM cycle ergometry tests. When compared to the true VO_2max values, the ACSM test overestimated VO_2 in 85% of the subjects, with a percent error of 25% (21). The protocol used by Griewe et al was outlined in the 1991 ACSM Guidelines and although current for the time, has since been updated. The latest edition of the ACSM Guidelines has once again published a new, modified protocol that will be evaluated in the present thesis. The most recent version involves progressively increasing the workload during four 3-minute stages (43). The use of 3-minute stages as compared to the 2-minute stages in the previous protocol gives the subject's heart rate an extra minute to reach steady-state prior to the increase in workload. Also, the newer version allows the subject to work at up to 85% of their maximum age-predicted heart rate (43) resulting in a more precise extrapolation and maximal exercise intensity. Both of the modifications combine to offer a more subject-specific protocol where predicted VO_2max values should be closer to measured ones. Other than the previously-mentioned studies of the 4th edition protocol, there has only been one other published study that reported only the validity, of the most recent ACSM submaximal cycle ergometry protocol. Stanforth et al measured the accuracy of the ACSM submaximal cycle ergometry test versus the equations of Berry et al, Lang et al, Latin and Berg, Londeree et al and its own Heritage-1 equation (61). It was found that after 20 weeks of training on a cycle ergometer, the ACSM equation was the only

equation to produce estimated VO_2max values that were not significantly different from the true measured values (61). Even though Stanforth et al verified the validity of the 5th edition ACSM equation with 715 men and women age 16-65, they did not analyze the reliability of its measurements and did not control for the female menstrual cycle. Therefore, this study will determine the reliability and validity of estimated VO_2max values from the 5th edition ACSM testing protocol and equation for women on oral contraceptives.

In 1993, Latin and Berg revised the 4th edition ACSM equation for estimating the O_2 cost of exercise performed by young women on a cycle ergometer (34). The new revised equation was based on a VO_2/power relationship, rather than heart rate. The validation test required the actual measurement of gases to monitor steady rate oxygen consumption. Once a steady rate was maintained at a certain workload, the workload was increased to the next stage. The test advanced to the following stages: 180, 360, 540, and 720 kgm/min. Completion of the test occurred when the subject reached 85% of their maximum heart rate (220-age) or finished the final stage (34). Latin and Berg, although using the ACSM testing protocol and equation as a basis, designed the following resulting equation:

$$VO_2(\text{ml/min}) = \text{kgm/min} \times 1.6 \text{ ml/min} + ((3.5 \text{ ml/kg}\cdot\text{min} \times \text{kg body weight}) + 205 \text{ ml/min}$$

The Latin and Berg equation was found to provide submaximal predicted values in young women that were closer to maximal treadmill results, when compared to the ACSM equation. The designers attributed this greater accuracy to the fact that the

equation was based on an actual VO_2/power relationship in women. They also found higher correlation values between their modified equation and actual VO_2max values at each workload. Since the Latin and Berg equation was designed for young women similar to our subject population, the analysis of this thesis will include the original 5th edition ACSM equation predicted value along with the results of the revised Latin and Berg equation as applied to our subject's data.

Prior to its publication in next year's 6th edition of the ACSM Guidelines, a new cycle ergometry equation has been developed (31). It uses the exact same testing protocol as the 5th edition ACSM equation and therefore its validity was also analyzed in this thesis. Since the equation's accuracy hasn't been verified and changes could occur prior to its actual publishing date of February 2000, this thesis will refer to it as the prospective ACSM equation or (ACSM new). The prospective ACSM equation:

$$VO_2(\text{ml/min}) = 1.8\ (\text{work rate in kgm/min}) \bullet (\text{kg body weight})^{-1} + 7\ \text{ml/min}$$

<u>Treadmill vs. Cycle Ergometer Maximal Exercise</u>

To compare the results of a submaximal cycle ergometry test to a measured VO_2max test, both a cycle ergometer and maximal treadmill have been used. Although using a cycle ergometer for both tests can control mechanical efficiency, it has been found that only a peak VO_2 is reached on a bike, rather than a true VO_2max (43). The "Gold Standard" is known as maximal treadmill testing (60) because it is much harder to get individuals to reach their maximal aerobic capacity on a cycle ergometer unless they

are cyclists, while obtaining a true VO_2max on a treadmill is more likely (14). On a treadmill, the test does not depend on the strength or fatigue-resistance of the quadriceps muscles. Treadmill maximal values are usually higher, and are therefore a true VO_2max, relative to cycle ergometry maximal levels, because of the greater muscle mass involved in treadmill walking or running (50). In 1997, Lockwood et al compared a maximal treadmill test to the results of two submaximal cycle ergometry prediction tests (the AF and progressive cycle (PROG) tests) because the maximal treadmill test is the "Gold Standard" (40). In another study, both cycle ergometry and treadmill maximums were used to compare predicted values from a submaximal cycle ergometry test. They found an 8.5% overestimation in the predicted value as compared to the maximal treadmill test and an 18.5% overestimation when prediction results were compared to the maximal cycle ergometer test (24). According to Fernhall and Kohrt, cycle ergometry VO_2max values are 10-15% lower than those obtained from a maximal test on a treadmill (16). The difference has been attributed to the failure of reaching a true VO_2max on the cycle ergometer.

<u>The Menstrual Cycle and Oral Contraceptives</u>

Oral contraceptives (OC) are prescribed to women for a variety of therapeutic reasons. Recently more and more women, especially in the military, are using them for the convenience they offer in regulating menstrual cycles, controlling menstrual symptoms and preventing conception. Original formulations contained higher dosages of both estrogens and progestins, however current OC contain lower doses of synthetic

hormones (35). These synthetic hormones are taken for 21 days (Q-L), creating a lengthened luteal phase with high progestin levels, followed by one week of taking a placebo pill (Q-F), similar to the follicular phase when menses occurs. The synthetic sex hormones in OC seem to mimic the physiological actions of their endogenous counterparts. However, to what extent is unknown. Like endogenous estrogen and progesterone, research has shown that the synthetic estrogens and progestins in OC can alter a female's physiological response to exercise (6, 11, 22, 36, 49).

In normally menstruating women, body core temperature is 0.2-0.6° C higher during the luteal phase, when progesterone levels are high, than during the follicular phase (8, 22, 26, 42, 54). Evidence suggests that the rise in body core temperature is due to the increased concentration of endogenous progesterone seen in the luteal phase (26, 28, 54, 62). It has been suggested that the synthetic progestins, found in OC pills, can be equally as potent in their thermoregulatory effects on female body temperature as their endogenous counterparts (54). Just like endogenous progesterone, the progestin component of the pill has been found to have the dominant effect on thermoregulation because during the quasi-luteal (Q-L) phase of the pill cycle, female core body temperature is higher than in the quasi-follicular phase (Q-F) (22, 54).

Although not all researchers agree, studies have shown that during both submaximal and maximal exercise there are significant differences in heart rate between the luteal and follicular phases of the menstrual cycle (26, 52, 56). Pivarnik et al studied the menstrual cycle phase effects of temperature regulation during endurance exercise in nine active women. They found higher exercising heart rates (by 10 beats/min) in the luteal phase, when progesterone and body temperature levels were high, in eight of their

subjects. However the single subject who failed to ovulate during testing, which inhibited the increase in progesterone, did not demonstrate a significantly higher exercising heart rate or body temperature in the luteal phase. Therefore, Pivarnik et al postulated that the progesterone-induced higher core body temperature during the luteal phase caused a secondary increase in cardiovascular strain during exercise causing an increased heart rate (52). Hessemer and Bruck measured 10 women's thermoregulatory responses to 15-minutes of exercise at night (between 0300 and 0400 hours) in both phases of the menstrual cycle. They also found that the increased body core temperature in the luteal phase enhanced heart rate response by 6 beats/min (26). In still another study, Schoene et al found that maximum heart rates in both trained and untrained women were significantly higher in the luteal phase (179 ± 2.9 compared to 185 ± 3.5) (56). However, many other researchers have concluded that the menstrual cycle does not affect heart rate response during exercise. Horvath and Drinkwater concluded that hormones do not influence female response to exercise in the heat, after measuring thermoregulatory variables in four women during submaximal treadmill exercise. A similar heart rate response to exercise in three heat environments was found regardless of the endogenous progesterone and estrogen concentrations (28). While testing the differences between menstrual phase and menstrual status in eight eumenhorreic and amenhorrheic women, DeSouza found no differences in maximum exercising heart rates (13). When analyzing the differences in vasodilation between the phases of the menstrual cycle in four women, Hirata et al found a significantly higher core body temperature in the luteal phase but no differences in exercising heart rate (27). The majority of studies have not demonstrated any substantial alterations in exercising heart rate during the

menstrual cycle (13, 15, 30, 37, 48). However, small subject numbers (between 4 and 9) used by the previously mentioned studies might have decreased the power of the statistical tests to find significant differences when they actually did exist.

In 1997, Rogers and Baker measured the thermoregulatory responses of seven women using OC. During the Q-L phase the subjects had an elevated heart rate by approximately 6-7 beats/min during exercise as compared to their heart rate response in the Q-F phase (54). The authors suggested that the subject's elevated body core temperature, which was significantly higher during the Q-L phase and most likely mediated by the synthetic progestin, caused the increase in heart rate (54). However, another study found that heart rate increased similarly in response to exercise during the two phases (22) and one study found that heart rate actually increased in the Q-F phase, however this was during heat stress and not exercise (10). While using the same women as their own control, Hartard et al found that heart rate was decreased during exercise in the Q-L phase when compared to the subject's heart rate response to testing in the luteal phase of a normal menstrual cycle (23). Another study found no difference in heart rate, however the subjects were tested twice during the Q-L phase, during the first week of taking the pill and then one week later (42). Finally, a study by Walters and Lim found that blood pressure and cardiac output increased during submaximal exercise in women on OC for 2-3 months, with no increase in heart rate (66). The variability in heart rate responses in women using OC is a cause for more study because more and more active women are using OC.

In regard to exercise performance during OC use, several studies have measured the effects of OC on maximal aerobic capacity. Daggett et al measured the effects of OC

administration by testing women before, during and 6 weeks after 2 months of OC use. During OC use, a decrease in VO_2max and muscle mitochondrial citrate was reported. However, the changes returned to normal by 6 weeks post-cessation of the medication suggesting that the synthetic hormones in the OC were the reason for the decreased performance (11). In a longitudinal study, Notelovitz et al monitored the exercise performance of 6 OC users and 6 normal women over a 6-month period. They found a 7-8% decline in the maximal aerobic capacity of subjects on OC only and found that all values returned to normal one month after stopping the use of OC (49). Lebrun et al tested 14 elite female athletes during one ovulatory menstrual cycle (both luteal and follicular phases) and then retested subjects during OC use. There was a slight decrease in the VO_2max values from the follicular to the luteal phase which decreased even further, to a 5% decrease in maximal aerobic capacity, after 2 months on OC (36). Therefore, research suggests that the administration of exogenous steroid hormones may have a slight detrimental effect on aerobic capacity.

Many different pill formulations are available consisting of various combinations of estrogens and progestins. The specific effects that each of the synthetic estrogens and progestins have under resting conditions and during exercise are unknown. Since the 1980's there have been advancements in oral contraceptive formulation research and lower-dose preparations have become available (35). Each previously mentioned OC study tested women of different fitness levels who were using a wide range of different pill types, from older high-dose OC to the latest low-dose formulations containing the newest progestins. Therefore, interpretations of OC studies are further complicated by

the diversity in the synthetic hormone components of the oral contraceptives used, as well as in the range of fitness of the individuals involved (35).

Purpose of this Study

The number of military women using oral contraceptives is increasing. Based on previous research, it is reasonable to suggest that the synthetic hormones in OC can possibly alter heart rate during mandatory submaximal cycle ergometry tests that rely on a heart rate-VO_2 linear relationship. Not one previous validation study has controlled for the menstrual cycle or oral contraceptive use. Therefore, a question arises as to the reliability and validity of a cycle ergometry test for women on oral contraceptives. This can be important if predicted levels are wrong and qualified women are failing the test and not qualifying for specific jobs. It can also be detrimental if underqualified women are passing the test when they have not achieved a certain level of fitness. It is also important to determine whether different types of oral contraceptives will provide alternate results during submaximal testing. The purpose of this study (as previously mentioned) was to analyze the validity and reliability of two submaximal, heart rate-dependent cycle ergometry tests as predictors for VO_2max in women on OC- using both the Air Force modified A-R protocol and the ACSM submaximal testing protocol. Values within ± 5% of actual measured VO_2max were considered valid and reliability was determined by the consistency between the two measurements in each phase of the cycle. This study also assessed the effect of oral contraceptives, particularly progesterone-like synthetics, on heart rate during submaximal exercise.

Chapter 3

EXPERIMENTAL METHODOLOGY

Subjects

Eighteen healthy women (19-22 years of age) of average fitness (3-5 days per week of aerobic activity) were recruited for this study (refer to Table 3 for characteristics). Approval for the research protocol was obtained from the Penn State University Institutional Review Board. Each subject signed an informed consent form, that outlined the nature and details of the study, filled out a personal information summary sheet and answered a health questionnaire (copies included in the appendix). Subjects were given a thermometer and a temperature chart to record their early morning temperature through one month (or one cycle). This was done to ensure that a distinct temperature pattern was noted between the Q-F and Q-L phases. Each subject reported for testing dressed in appropriate exercise clothing and having complied with the following predetermined guidelines (also used prior to AF testing):

- No eating within 1 hour of the test (a recommended breakfast of cereal and toast)
- No caffeine within 12 hours
- No alcohol within 24 hours

- Minimum of 6 hours sleep the night before (8 hours recommended)
- No other medication taken (definitely no β blockers)
- No aspirin taken 24 hours prior to testing
- Subjects have had one year of continual oral contraceptive use

	Mean	SD	Range
Age (years)	20.6	0.2	19-22
Mass (kg)	60.3	1.6	50.7-73.8
Height (cm)	164.9	1.00	158-173

Table 3. Characteristics of Subjects

None of the subjects smoked and all but one had been using OC for one year or more (one subject had been on OC for 10 months). Eleven different OC formulations, with differing amounts of synthetic hormones were used by the women in this study (refer to Table 4). All of the pills contained the same estrogen component, ethinyl estradiol, in similar amounts (between 20 and 40 μg). However the synthetic progestin components, some of which are structurally similar (levonorgestrel, norethindrone, noregestimate, noegestrol, ethinodiol diacetate and desogestrel) accounted for the differences between pill types. The 11 OC formulations were then compacted into 4 structurally related categories based on the synthetic progestins. These groups paired norgestimate with levonorgestrel and ethinodiol diacetate with norethindrone, leaving desogestrel and noegestrol in each of their own groups. After further analysis of the temperature curves throughout one pill cycle, the pill types were regrouped based on their influence on body temperature (Table 5). Although pills were similar, differences in formulations were taken into consideration statistically in the results section.

Oral Contraceptive	*n*	Days	Estrogen (mg)	Progestin (mg)
Ortho-Novum 7/7/7	1	1-7	0.035 EE	0.50 NET
		8-14	0.035 EE	1.00 NET
		15-21	0.035 EE	0.50 NET
Loestrin	1	1-7	0.020 EE	1.00 NET
		8-21	0.020 EE	1.50 NET
Ortho-Tricyclen	5	1-7	0.035 EE	0.180 NGM
		8-14	0.035 EE	0.215 NGM
		15-21	0.035 EE	0.250 NGM
Ortho-cyclen	2	1-21	0.035 EE	0.250 NGM
Triphasil	2	1-6	0.030 EE	0.050 LNG
		7-11	0.040 EE	0.075 LNG
		12-21	0.030 EE	0.125 LNG
Tri-levlin	2	1-6	0.030 EE	0.050 LNG
		7-11	0.040 EE	0.075 LNG
		12-21	0.030 EE	0.125 LNG
Nordette	1	1-21	0.030 EE	0.150 LNG
Levora-28	1	1-21	0.030 EE	0.150 LNG
Lo/Ovral	1	1-21	0.030 EE	0.150 NGL
Demulen	1	1-21	0.035 EE	1.00 EDT
Ortho-cept 28	1	1-21	0.030 EE	0.150 DGL

Table 4. Oral Contraceptive Formulations: The synthetic steroid content of each of the OC used by the subjects in this study, where "*n*" is the number of subjects in the study on that specific OC and "Days" identifies the dosage regimen. Tri-levlin, Tri-phasil, Ortho-tri-cyclen and Ortho Novum are tri-phasic pills where the amount of hormone in each pill varies across the 21-day cycle. Each pill cycle consists of the individual taking one synthetic hormone pill each day for 21 days followed by 7 days of taking a placebo pill. Day 1 denotes the first day the subject starts a new packet of pills. NET= Norethindrone, NGM= Noregestimate, LNG= Levonorgestrel, NGL= Noegestrol, EDT= Ethinodiol Diacetate, DGL= Desogestrel

Progestin	OC
Norgestimate *n*=7	Ortho-tricyclen and Ortho-cyclen
Levonorgestrel *n*=5	Nordette, Tri-phasil, Tri-levlin and Levora-28
Ethinodiol Diacetate and Norethindrone *n*=3	Demulen, Ortho-Novum 7/7/7 and Loestrin
Noegestrol and Desogestrel *n*=2	Lo/Ovral and Ortho-cept 28

Table 5. Oral Contraceptives Grouped Based on Similar Temperature Profiles

Testing

Two phases, a quasi-follicular (Q-F) and a quasi-luteal (Q-L) were identified in the 28-day cycle (refer to Figure 1). Subjects were tested between days 8-15 of the 21-day period of taking pills (Q-L) and two weeks later, days 26-28 (Q-F), when placebo pills were being taken. The 3-day window in the quasi-follicular phase allowed testing to be conducted after 4 days of the subject not taking hormones, ensuring maximal clearance of the synthetic hormones from the bloodstream. In each phase, a maximal test was conducted one day followed by a day of rest and then a day of submaximal testing. The two submaximal tests (AF cycle ergometry and ACSM) occurred on the same day with a 30-minute rest period in between. Oral temperatures, height and weight were taken immediately prior to all testing. Testing was conducted at the same time of day, in the morning (approximately 0700-1200 hours) on testing days. A random order was assigned according to each woman's individual menstrual cycle, where some subjects were tested in the Q-F phase first while others were tested in the Q-L phase first. Also, the order of the submaximal tests were randomized between subjects, but kept consistent for each subject between phases. Rating of Perceived Exertion (RPE) (7) measurements were recorded.

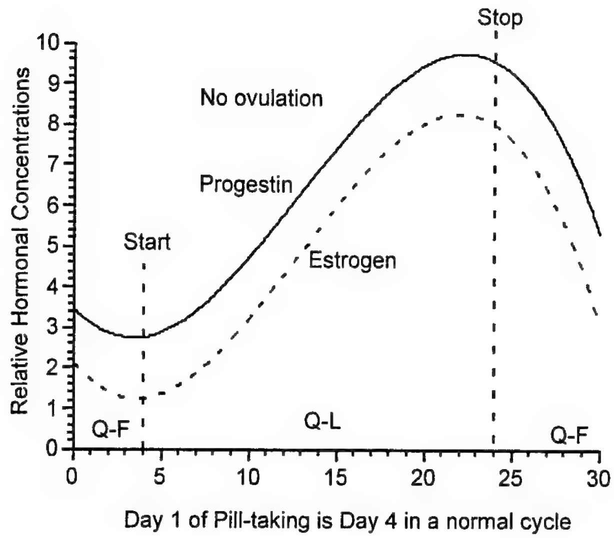

Figure 1. Hormonal Fluctuations during the OC Menstrual Cycle

Maximal Treadmill Testing

To determine maximum O_2 uptake, subjects were tested to physical exhaustion. Tests were terminated when subjects met two of the following four criteria: 1) attained a leveling of VO_2 although workload increased, 2) the subject's heart rate reached age-predicted maximum, 3) the R (Respiratory Exchange Ratio) reached 1.1 or higher (40) or 4) volitional exhaustion or an RPE of 19 or 20.

Maximal tests were performed on either of two types of treadmills. One treadmill, the Precor USA C962 was set to increase by 2% increments in grade while the other, the Quinton Instruments Company Model #18-60-1, was set for 2.5% increases in grade. The test protocol was designed to progressively increase the subject's work intensity until an exhaustive state was reached. In brief, subjects performed a warm-up walk on a 0% grade at 3.0 mph for 2 minutes. This was followed by a 1-minute warm-up run on a 0%

grade at either 5.5 or 6 mph (dependent on the individual's reported activity level). Every 2 minutes the grade was increased by 2-2.5% depending on which treadmill was used. This continued until exhaustion and the previously mentioned criteria were met. All subjects (n=18) attained at least two of the four criteria during maximal testing. A 12-lead electrocardiogram (Marquette Electronics EKG) was used to measure and monitor heart rate while gases (O_2 and CO_2) were measured using a dry-gas meter, a Beckman CO2 Medical Gas Analyzer LB-2, and an Applied Electrochemistry Incorporated O2 Analyzer.

Submaximal Cycle Ergometry Tests

Submaximal tests occurred between 24 and 72 hours after maximal exercise testing. Due to scheduling conflicts, it was impossible to have all 18 subjects report for their submaximal testing 48 hours after the maximal test. Therefore, five subjects came in 24 hours after and three subjects came 72 hours after maximal exercise testing during one testing phase. A random order was assigned as to which test would be completed first, the ACSM or the AF. A minimum of 20 and up to 35 minutes was used as resting time between the two tests. Subjects were instructed to bring in a first morning sample of urine on each day of submaximal testing. An antecubital venous blood sample was also taken just before the first test began. The collected blood was used in a related study for measurements not reported in this text. Prior to testing, subjects were properly positioned on an 818E Monark cycle ergometer with upright posture, 5° bend in the knee at maximal leg extension and hands placed in the proper resting position on the handlebars. Subjects

were then asked to warm-up at 0.5 kp for 2 minutes prior to starting the tests. Expired gas measurements were measured as before and a 12-lead EKG monitored heart rate. A cool down period of 5 minutes at 0.5 kp was initiated at the completion of the test.

Submaximal Cycle Ergometry Test #1 (AF cycle ergometry)

The starting workload was calculated using age, sex, body weight and exercise history (See Table 6**). Subjects began pedaling at 50 rpm and maintained this rate throughout the test. The workload was increased until a steady-state heart rate between 130-150 bpm was achieved (See Table 7**). Subjects worked between 6 and 14 minutes, reaching a heart rate that did not fluctuate ± 5 bpm over 2 consecutive minutes during a 6-minute constant workload setting. When this steady-state occurred, the test was terminated. The steady state heart rate, which was the average of the last two heart rate readings and final workload values from the test, was entered into the AF Fit-Soft software containing the AF cycle ergometry test program (60). The computer program used a computation containing age, weight, height, average ending heart rate, a conversion constant for body surface area and final workload to calculate each subject's predicted VO_2max (25).

Weight	<54.88 kg		<63.95 kg		<73.02 kg		<82.09 kg	
Exercise History	Active	Inactive	Active	Inactive	Active	Inactive	Active	Inactive
Workload (kp)	1.0	1.0	1.5	1.0	1.5	1.0	2.0	1.5

Table 6. Initial Workload Cycle Settings for Females aged 17-35

Workload	+ 1 kp			+ 0.5 kp			+ 0.0 kp			Terminate
Minute	4	6	8	4	6	8	4	6	8	
Heart Rate	<110	<110	<115	110-119	110-119	115-128	120-173	120-173	129-173	HR> 85% of max

Table 7. Progression Workload Cycle Changes for Females aged 17-35*

*Note: Heart rates used to determine workload progression are taken at the end of the minute. For example, minute four of the test is performed at the initial workload, with the heart rate at the end of minute four (3:55) determining the workload progression for minute five using the “Minute 4” workload progression column. The heart rate at the end of the sixth minute (5:55) would then determine the workload progression for minute 7 using the “Minute 6” workload progression column.

*Note: If at minute 8 there have been 6 constant workloads and any last three heart rates were 125 or greater (in steady state) the test should be terminated. Otherwise, continue the test and increase the workload according to the chart.

**Note: The above tables contain testing parameters pertaining to subjects in the present study only. The above information was used with permission from the Air Force Exercise Physiology Laboratory, Brooks AFB, TX.

Submaximal Cycle Ergometry Test #2 (ACSM)

The ACSM cycle ergometry test protocol consists of 3-minute stages with appropriate increments in workload. The present study used 4 separate stages in which workload was increased from 0.5 kp to 1.5 kp to 2.0 kp and to 2.5 kp. Heart rate was monitored and recorded via EKG during the last 15 seconds of each minute in each 3-minute stage. This was done to ensure that a steady state heart rate was achieved prior to the increase in workload. A constant pedal speed of 50 rpm was maintained throughout the test. The test was terminated at the end of the fourth stage. The final heart rate at each workload was then used to determine a linear regression line to the maximum age-predicted heart rate. This corresponded to a maximal exercise intensity from which VO_2max was estimated. The following is the equation used to determine the ACSM predicted value:

$$VO_2 \text{ (ml/min)} = 3.5\text{ml/kg}\cdot\text{min x kg body weight} + 2.0 \text{ x power output (kgm/min)}$$

Prior to the publishing date of the 6th edition of the *ACSM's Guidelines for Exercise Testing and Prescription*, the investigators of this study were notified of a modification to the ACSM equation that will be published in the new edition of the ACSM Guidelines. The prospective ACSM equation reads as follows:

$$VO_2 \text{ (ml/min)} = (1.8 \text{ ml/kg}\cdot\text{min x work rate (kg}\cdot\text{m/min))} \cdot \text{(kg body weight)}^{-1} + 7 \text{ ml/min}$$

Statistical Analysis

Submaximal heart rates from the ACSM test were extrapolated to age-predicted maximum heart rate by linear regression. To compare the estimates of VO_2max from the ACSM equations and the AF test to true VO_2max, paired t-tests were used. Also, to compare temperatures between phases, R at a constant workload and VO_2 at a constant workload, paired t-tests were used. A paired t-test was also used to assess the reliability of the AF and ACSM tests across the two phases. Standard error of the mean was calculated in all situations, as well as correlation coefficients. Percent error of the predicted value from the measured VO_2 max was found using the equation ((estimated-measured)/measured*100). Analysis of variance (ANOVA) was used to determine phase-related differences in heart rate, temperature, estrogen content of the pill, true max, the AF test, the ACSM equation and the new ACSM equation between the pill groups. ANOVA was also used to determine the phase-related differences in heart rate at the various workloads of the ACSM test. The level of statistical significance was set at the alpha level of 0.05.

Chapter 4

RESULTS

A total of 18 women were recruited for this study, however only 17 are included in these results. One subject's data was unusable due to an incomplete test in the Q-F phase and an unexpected sickness that required antibiotics. Testing was randomized between phases (8 subjects tested in the Q-L phase first and 9 subjects tested in the Q-F phase first) and between submaximal tests (9 subjects completed the AF test first and 8 subjects completed the ACSM test first).

Body Temperature

Each subject plotted her temperature on a chart for one 28-day menstrual cycle. This was done in order to determine the efficacy of the pill by ensuring that a definite temperature difference existed between the Q-F and Q-L phases. These temperature charts were also used to determine similar biological effects among the eleven different pill formulations used by the subjects in this study. Patterns were noted by separating each subject into one of four pill formulation categories: Group P1 (n=7) progestin: norgestimate, Group P2 (n=5) progestin: levonorgestrel, Group P3 (n=3) progestins: norethindrone and ethinodiol diacetate and Group P4 (n=2) progestins: noegestrol and

desogestrel. Each group had a cyclic pattern in which the lowest temperatures ranged from days 26-28 and days 1-4, with the highest temperatures peaking around day 20 (Figure 2). Significant, pill-related differences in temperature curves across the entire 28-day cycle (P = 0.002) were observed and among each pill type, the cycles themselves were significantly different between the Q-L and Q-F phases (P=0.0001). Due to small group numbers and the same cyclic pattern noted in all four groups, only the average temperature curve was plotted (Figure 2). However, overall P1 had the lowest temperature curve that was significantly different from P2 (P=0.0007) and P4 (P=0.0016). There was also a significant difference (P=0.009) in the morning of testing temperature values (°C) between the Q-L and Q-F phases (Q-L = 36.4 ± 0.077, Q-F = 36.1 ± 0.087). The estrogen content of the pills did not contribute to the significant differences in temperature that was seen between pill types, as determined by ANOVA.

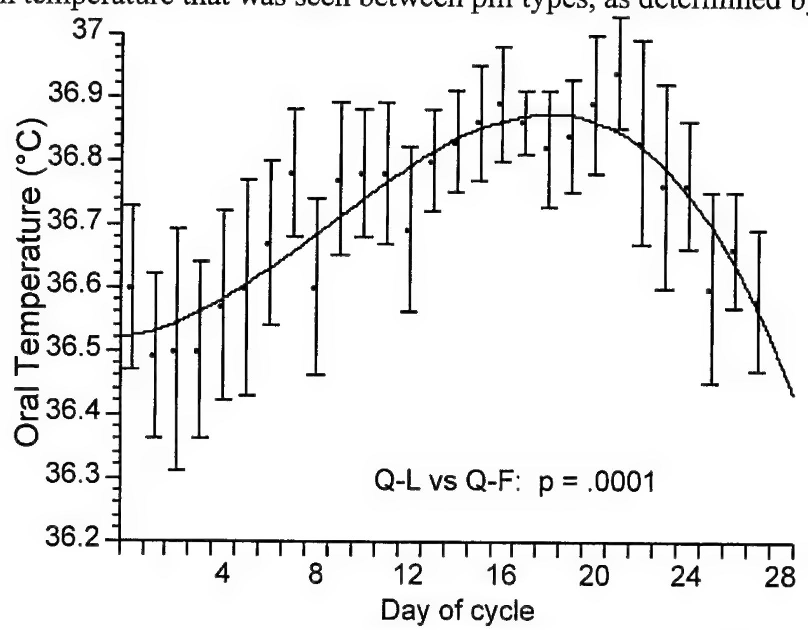

Figure 2. Mean oral temperature, from each subject's chart, as a function of time over the course of the 28-day controlled menstrual cycle during oral contraceptive use. Values are expressed as means ± SE. A significant difference in the temperature curve was found between the Q-L (Days 1-21) and Q-F (Days 22-28) phases.

Maximal Treadmill Test

The VO_2max test was lower (by 1.1 ± 0.63 ml•kg^{-1}•min^{-1}) in Q-L than in Q-F (Q-L= 38.2 ± 1.1 ml•kg^{-1}•min^{-1}, Q-F= 39.3 ± 1.1 ml•kg^{-1}•min^{-1}, P=0.055, Figure 3). Eleven women showed an increase in VO_2max in the Q-F phase and 6 showed a decrease relative to the Q-L phase. This increase was not specific to pill type.

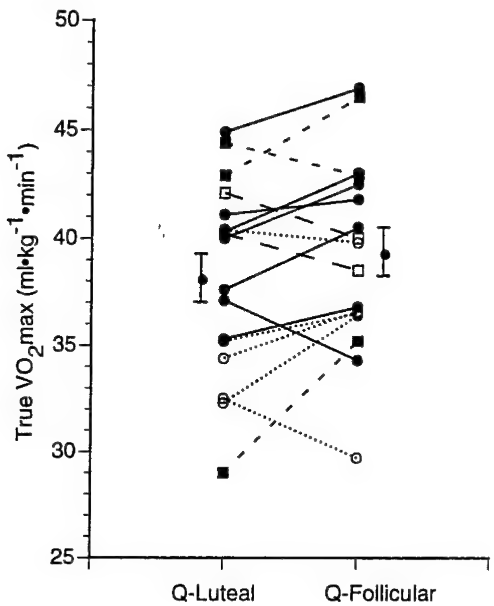

Figure 3. The effect of oral contraceptive cycle phase on maximal aerobic capacity. Different pill types are noted by symbols.

Validity and Reliability of the Air Force Test

Comparison of the AF submaximal cycle ergometry test to the maximal values reveals a slight, non-significant (1.5%) overestimation in the Q-L phase (AF= 38.8 ± 1.8 ml•kg^{-1}•min^{-1} vs. Max= 38.2 ± 1.1 ml•kg^{-1}•min^{-1}, P=0.3) and a larger underestimation (5%) in the Q-F phase (AF= 37.4 ± 1.8 ml•kg^{-1}•min^{-1} vs. Max= 39.3 ± 1.1 ml•kg^{-1}•min^{-1},

(5%) in the Q-F phase (AF= 37.4 ± 1.8 ml•kg^{-1}•min^{-1} vs. Max= 39.3 ± 1.1 ml•kg^{-1}•min^{-1}, P=0.06, Figures 4 and 5.1). Figure 5 displays graphically the relationship between the VO_2max estimates and the measured VO_2max values for each of the 3 equations in both phases of testing, including the r and p values. Graph 5.1 shows the differences between the Q-F and Q-L AF tests. The AF test in the Q-F phase had both a higher correlation and lower SE than the Q-L test, however the majority of the estimates produced values below the line of identity, representing an underestimation of VO_2max. As shown in Figure 6, both of the tests were within the ± 5% validity range used in this study's testing protocol. There were no significant differences in average R or VO_2 between the Q-L and Q-F phases for the AF test. There was a significant difference (P<0.05) between the predicted VO_2max values of the AF test between the two phases (Q-L= 38.8 ± 1.8 ml•kg^{-1}•min^{-1}, Q-F= 37.4 ±1.8 ml•kg^{-1}•min^{-1}, P=0.02) and also between the final average heart rates used to calculate the predicted VO_2max values (Q-L= 141.5 ± 3.4, Q-F= 147.6 ± 3.6, P=0.003).

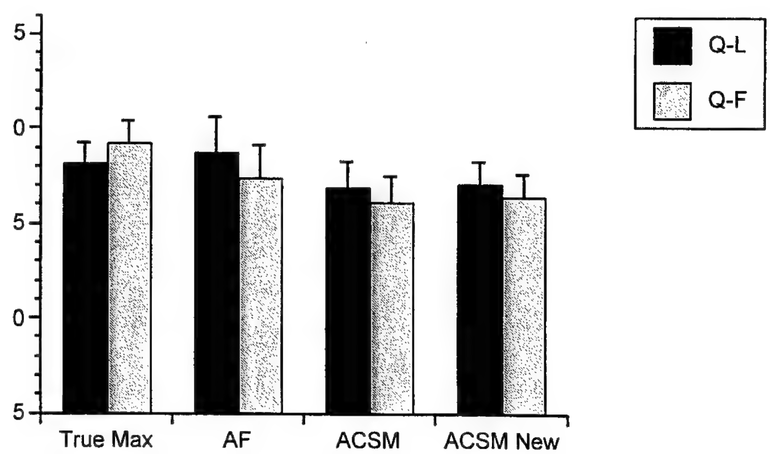

Figure 4. Comparison of VO_2max (mean and SE) estimated using submaximal cycle ergometry tests (AF and ACSM) and measured during maximal treadmill exercise.

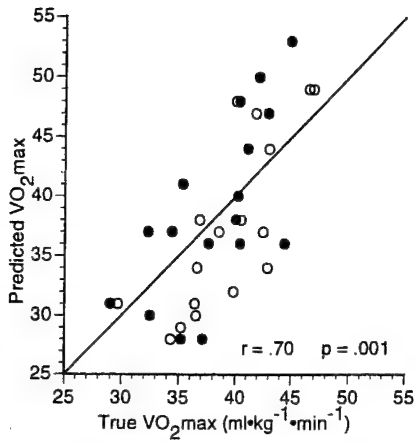

Figure 5.1 AF Test

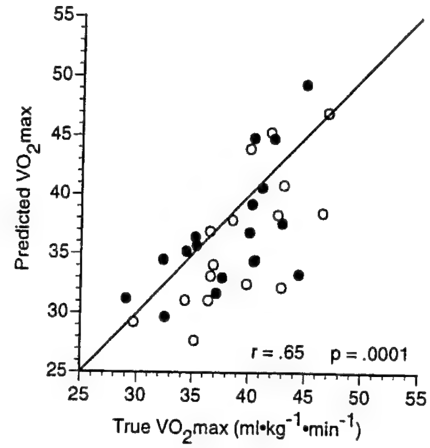

Figure 5.2 ACSM Test

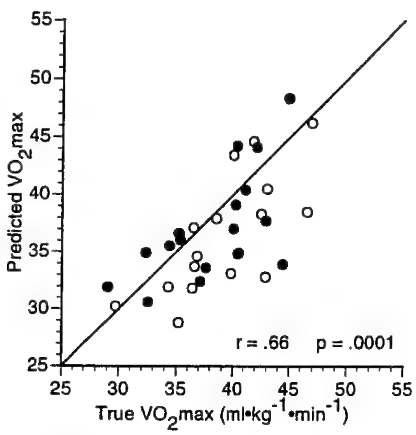

Figure 5.3 ACSM New

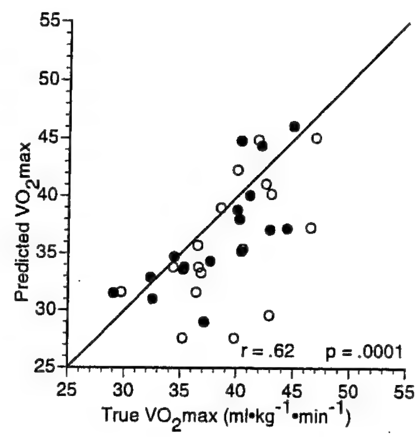

Figure 5.4 ACSM using True HR

Figure 5. Graphic display of the relationship between VO_2max estimates and the measured VO_2max values for each of the equations. Closed circles = Q-L and open circles = Q-F.

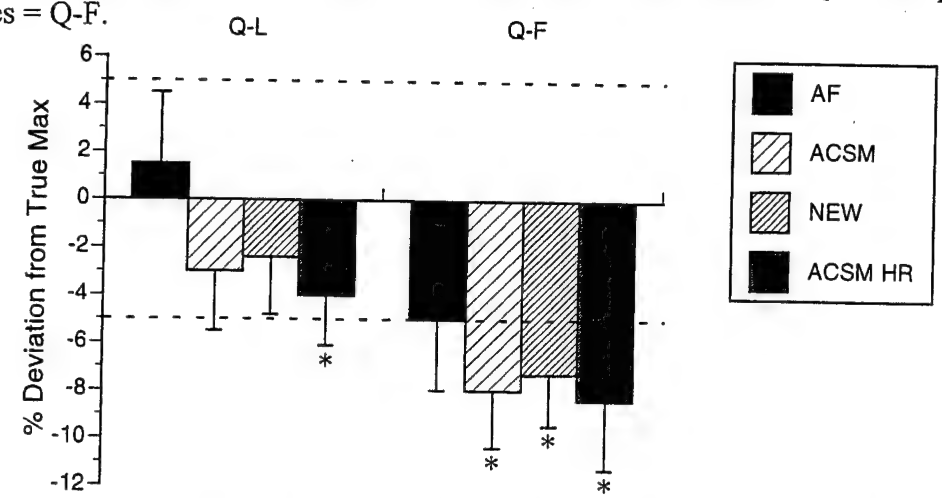

Figure 6. Differences in estimated and measured oxygen uptake expressed as a percent of the measured oxygen uptake. * Denotes significance from measured value.

Validity and Reliability of the ACSM Test

The comparisons between the maximal test values and the ACSM cycle ergometry test resulted in a statistically significant difference only in the Q-F phase (Q-F= 36.1 ± 1.4 ml•kg^{-1}•min^{-1} vs. Max= 39.3 ± 1.1 ml•kg^{-1}•min^{-1}, P=0.003- Figure 4). In both phases however, the ACSM test underestimated VO_2max, Q-L (3%) and Q-F (8%), as shown in Figure 5.2 and 6. In comparison to the AF test, the ACSM predicted values were lower and therefore more highly underestimated (Figures 4 and 6). There was a significant difference (P<0.05) in the heart rate data between phases. Since standardized workloads were used during the ACSM test only (at 0.5, 1.5, 2.0, and 2.5 kp), heart rate comparisons between phases were analyzed. In Figure 7, the Q-F heart rate curve was significantly higher (P=0.02) than the Q-L curve, across the entire workload sequence.

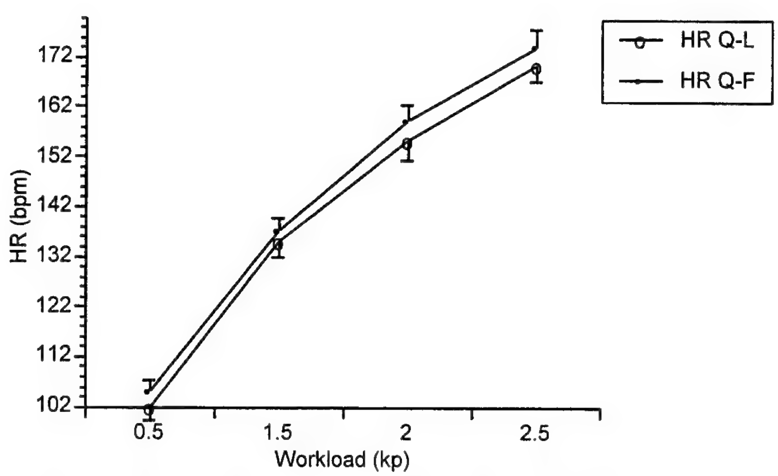

Figure 7. Mean heart rates at each workload during the ACSM test are plotted. The mean heart rate curve shows that heart rates were significantly higher in the Q-F phase as compared to the Q-L phase.

In the ACSM equation, submaximal heart rates are extrapolated to maximum age-predicted heart rate through the use of a linear regression line. Instead of using age-predicted max heart rate, actual measured max heart rate (recorded during the treadmill max test) was used to determine the predicted VO_2max value for the ACSM equation. This was done because previous research has suggested that estimated values are more accurate when the measured maximal heart rate is used, as opposed to the age-predicted maximal heart rate value. As shown in Figures 5.4 and 6, using the true maximal heart rate of the individual resulted in an even greater underprediction with a higher percent error of the estimated value compared to the ACSM equation using age-predicted maximal heart rate.

Validity and Reliability of the New ACSM Equation

When compared to the maximal values, as shown in Figures 4 and 6, the new ACSM equation underpredicted in both the Q-L (2.4%) and Q-F (7.3%) phase. Yet, it was a more reliable estimate of VO_2max than the original ACSM equation, by 0.17 and 0.24 $ml \bullet kg^{-1} \bullet min^{-1}$ in the Q-L and Q-F phases, respectively (Figure 6). There was no significant ($P>0.05$) difference from the measured VO_2max value in the Q-L phase, but the estimated values in the Q-F phase were significantly lower (Q-F= 36.4 ± 1.2 $ml \bullet kg^{-1} \bullet min^{-1}$ vs. Max= 39.3 ± 1.1 $ml \bullet kg^{-1} \bullet min^{-1}$, $P=0.003$- Figures 5.3 and 6).

Results Independent of Fitness Level

In order to be sure that the results for the AF and ACSM tests did not rely on the fitness level of the individual, the differences between the predicted value and the true VO_2max value were plotted versus true VO_2max. There were no evident patterns and no statistical significance between any of the predicted (AF, ACSM, ACSM new) and true VO_2max values in regards to fitness level. Therefore, fitness level was not a factor in determining the predictive ability of the submaximal tests studied in the present study.

The differences between the true VO_2max values in the two phases were also plotted versus the VO_2max in the Q-L phase and the VO_2max in the Q-F phase. No significant differences were noted for individuals at various fitness levels.

Body Weight

There were no significant changes in subject body weight (± 0.2 kg) between the Q-L and Q-F phases.

Results Between Pill Groups

The phase-related differences in heart rate (Figure 7), oral temperature taken the morning of testing, true VO_2 max, the measured values for the AF test, the original ACSM equation and the new ACSM equation did not depend upon the pill type. The predictive ability of all 3 submaximal cycle ergometry equations, as compared to true

maximal values in both the Q-L and Q-F phases, were not different due to pill type. All pill groups demonstrated higher heart rates in the Q-F phase therefore negating any specific heart rate effects to pill type. Although not statistically significant, due to small group numbers and large standard errors, Group P2 (n=5) had the highest heart rates while Group P4 (n=2) had the lowest heart rates in both phases of testing. However when looking at the change in heart rate between the Q-L and Q-F phases, there were no significant differences between pill groups. In comparing predictive values to maximal values, there was overall consistency since the predictive value for each of the three tests, across the 4 pill groups, was higher in the Q-L phase than in the Q-F phase. In regard to maximal test comparisons, Group P1 (n=7) had estimated values very close to the measured values for VO_2 max while Group P3 (n=3) seemed to contribute to the overall underestimation and Group P2 was probably the major contributor to the underestimation of values. Group P4 was the reason for the overestimation in the Q-L phase of the AF test and the balancing factor preventing the extreme underestimation of the ACSM equations. Group P4 was also the only group where the true VO_2max value was higher in the Q-L phase as compared to the Q-F phase.

Individual Results for the AF and New ACSM Equation

Figure 8 illustrates the individual deviations from the true VO_2max values (shown as a percent difference) for the AF test and new ACSM equations in both the Q-L and Q-F phases. Although the mean predicted VO_2max (by the AF test) was closest to true

VO_2max in the Q-L phase, the new ACSM equation resulted in more individual estimated VO_2max values that were within the ± 5% validity range.

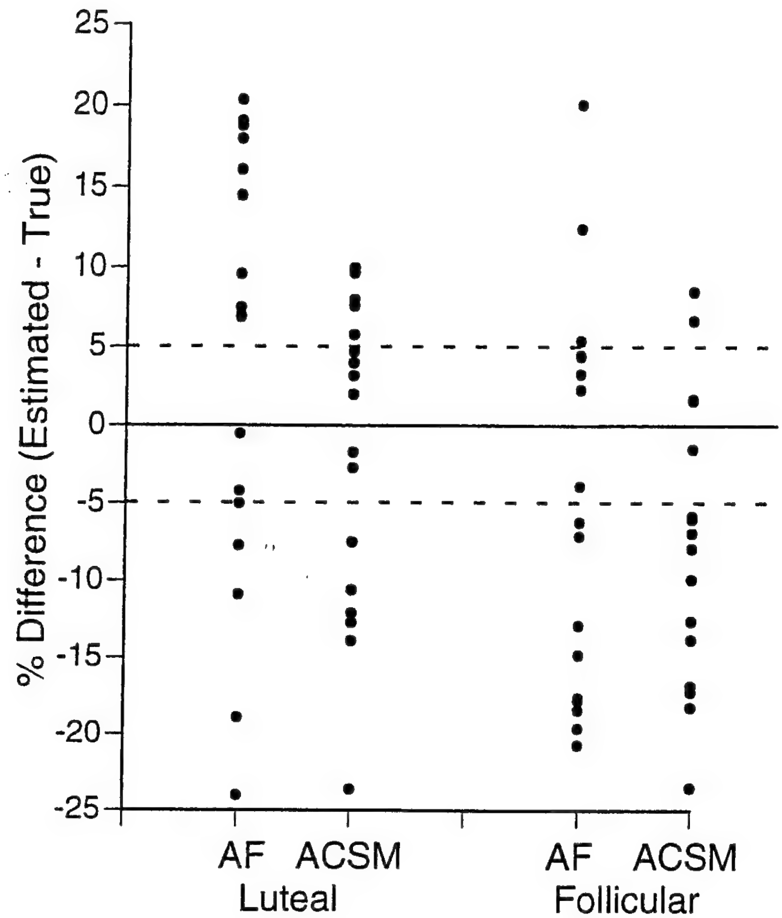

Figure 8. Individual differences in estimated and measured VO_2max values expressed as a percent of the measured oxygen uptake.

Fitness Rankings

In both the Q-F and Q-L phases, the AF test placed 41% of the subjects into the correct fitness categories according to their VO_2max values (Table 8). In the Q-L phase, 35% of the subjects were placed in a higher fitness category and 23% were placed in a lower fitness category than where they should be based on their true VO_2max values. In

the Q-F phase, the AF test incorrectly placed 52% of the subjects in a lower fitness category and only one subject was placed at a higher fitness level. Overall none of the subjects failed the test, in either phase, by receiving an estimated VO_2max value below 28 ml•kg^{-1}•min^{-1}.

For both the Q-L and Q-F phases, the new ACSM equation placed 57% of the subjects in a fitness category below where they should actually be placed. In the Q-F phase, 3 subjects were placed two fitness categories below their true classification. Only one subject, in the Q-L phase, was incorrectly placed into a higher fitness category. Therefore, although the ACSM test estimates exhibited fewer deviations from true VO_2max, the AF test resulted in more accurate placement in fitness categories.

PHASE	TEST	Equal	Under	Over
Q-L	AF	41%	23%	35%
Q-F	AF	41%	52%	6%
Q-L	ACSM	37%	57%	6%
Q-F	ACSM	41%	57%	0%

Table 8. The percent of subjects, using the estimated VO_2max values from the AF and new ACSM equations, that were placed in fitness categories equal, under or over the true classifications using measured VO_2max.

Chapter 5

DISCUSSION

This study sought to determine the validity and reliability of two submaximal cycle ergometry tests across a controlled menstrual cycle in young women using oral contraceptives. Based on the results, the AF submaximal cycle ergometry test based on the A-R nomogram is a valid predictor of maximal aerobic capacity for young women on OC. The ACSM cycle ergometry method of estimation also appears to be a valid predictor, with some reservations. The difference between the ACSM estimated VO_2max and the true VO_2max value was greater than the AF test results. The new ACSM equation should be used with the original protocol for the most accurate results. All three equations showed a difference in their predictions of maximal aerobic capacity between the two phases; therefore, submaximal testing cannot be reliably administered through an OC-controlled menstrual cycle. Thus, for the most valid results testing should occur in the Q-L phase. The phase-related differences in the estimated values is possibly related to a hormonal influence on the female heart rate response to submaximal exercise that needs to be further analyzed.

Maximal Treadmill Test

Maximal aerobic capacity was slightly higher (by 1.1 ± 0.63 ml•kg^{-1}•min^{-1}) in the Q-F phase (P=0.055). This is consistent with previous studies that have reported a decrease in VO_2max for subjects who begin taking oral contraceptives (11, 36, 49). The reasons for the differences in VO_2max values have been attributed to changes in body weight, substrate metabolism and possibly oxygen delivery to the tissues during the progression to maximal exercise. Daggett et al and Notelovitz et al tested women before, during and after OC use (0.035 mg of ethinyl estradiol and 0.4 mg of nerethindrone). They found a 7-8% decrease in VO_2max during OC use (Q-L phase testing) which returned to normal after cessation of the medication (11, 49). Notelovitz et al attributed this finding, in part, to the approximately 2-kg increase in weight gained by the women on OC (49). However, the present study only noted a weight difference of ± 0.2 kg between the two phases. The changes in substrate metabolism, stimulated by the OC pill, were the reason Daggett et al found a difference, but the present study did not measure the correct variables to draw a similar conclusion (11). Lebrun et al also measured a 5% decrease in VO_2max after 2 months on OC, with no effect on maximal heart rate (36). Hartard et al measured heart rate during submaximal cycle ergometry in 6 women during a normal menstrual cycle and a cycle on OC and found that heart rate decreased from the luteal phase of the normal cycle to the corresponding Q-L phase under OC use (23). This suggests that a decrease in heart rate at submaximal workloads could possibly decrease cardiac output and theoretically result in a decreased oxygen delivery to the tissues during the progression of exercise intensity in maximal testing during the Q-L phase.

This would result in a lower VO_2max value in the Q-L phase as compared to the Q-F phase, as seen in the present study.

There have also been a few studies that have found no maximal performance differences in OC users, leaving questions as to the reliability of testing methods, subject number and age, pill type, and exact phase of testing. Grucza et al found no performance differences between the Q-F and Q-L phases of young, fairly active OC users (22). But only 10 OC subjects were used and the maximal test was performed on a cycle ergometer which most likely resulted in a peak VO_2max value and not the true VO_2max of the individual (22). Some of these studies have compared VO_2max values from OC users tested twice during OC use (such as weeks 1 and 2 of pill taking in the Q-L phase) without testing in the placebo phase (42). The different synthetic hormonal levels experienced by a woman during the two different phases (Q-L and Q-F) could cause alterations in VO_2max performance and are therefore important to consider while testing, as the present study has shown. Yet, very few studies have looked at these differences and their effect on exercise performance, demonstrating the need for further analysis.

In contrast, in fairly active, normal menstruating women an abundance of evidence points toward insignificant variability in VO_2max between phases. However, Lebrun et al found a significant decrease in VO_2max during the luteal phase of the menstrual cycle in "trained" women ($0.06 \pm .03$ $l \bullet min^{-1}$) and Schoene et al. found the same result in non-athletic females (4.3 ± 2.7 $ml \bullet kg^{-1} \bullet min^{-1}$) (37, 56). Thus, it is also necessary to analyze the aerobic capacity of women on OC at varying levels of training status.

Submaximal Testing

Both of the established submaximal cycle ergometry tests, AF and ACSM, and the new ACSM equation significantly ($P<0.05$, except for the AF where $P=0.06$) underpredicted VO_2max in the Q-F phase by 5%, 8% and 7.3% respectively. In the corresponding Q-L phase, the AF test overpredicted (1.6%), the ACSM test underpredicted (3.3%), and the new ACSM equation underpredicted (2.9%) VO_2max demonstrating a higher validity in VO_2max estimations for all three equations in the Q-L phase as compared to the Q-F phase. Previous studies, which did not screen for menstrual cycle phase or oral contraceptive use reported a 15% underprediction for the A-R based AF test (12, 40, 50, 55). Also, previously noted overpredictions range up to 21% (24, 57, 58, 71). Thus, the validity of the estimated values as compared to the true maximal values is higher in this study as compared to the previous research.

However, Lockwood, Davies, Patton, Rowell and Siconolfi all used heterogeneous groups of subjects with differences in age and sex (12, 40, 50, 57, 58). Hartung et al used 37 women aged 19-47 and Zwiren et al used 38 women in their thirties (24, 71). The diverse subject pools used in these studies are most likely the reason for the vast difference between previously estimated values and those found in this study. The A-R nomogram was founded using an original validation group of 58 well-trained males and females between the ages of 18 and 30 (4). The 17 subjects used in this study were young (19-22 years of age), active women and their physical similarities to the A-R validation group probably contributed to the high validity of the A-R equation.

Previous research on the validity of the ACSM protocol and equation is fairly limited. Most of the research has focused on the equation and protocol from the 4th edition of the ACSM Guidelines, while this study tested the equation and protocol from the 5th edition of the ACSM Guidelines. Our protocol differed from other studies because we used four 3-minute stages where our subjects could reach up to 85% of their maximum age-predicted heart rate. These four values were then used to extrapolate to the maximum age-predicted heart rate value and thus the maximal exercise intensity from which an estimated VO_2max can be calculated. This is in comparison to the previous protocol that relied on four 2-minute stages and a maximum workload that allowed the subject to work at only 65-70% of their maximum age-predicted heart rate. The updated protocol is more reliable because 3-minute stages allow more time for the subject's heart rate to reach a steady state before workload is increased and less extrapolation is involved when subjects are able to work at a higher percentage of their maximum age-predicted heart rate.

There is only one study that analyzed the accuracy of the 5th edition ACSM prediction equation. Stanforth et al compared the ACSM to other submaximal prediction equations in 715 men and women aged 16-65, with no regard to female menstrual status (61). Each individual was tested prior to and right after completion of 20 weeks of cycle ergometry training (61). In pre-training, the ACSM equation significantly ($P<0.001$) underestimated VO_2max values while post-training, the ACSM equation generated values that were still lower but not significantly different ($P = 0.07$) from the measured values (61). Stanforth et al compared four different modified ACSM equations, Berry et al (1993), Lang et al (1992), Latin and Berg (1994), Londeree et al (1997) and one of their

own equations (Heritage-1) to the ACSM equation, from the 5^{th} edition of the ACSM Guidelines (61). The unmodified ACSM equation was the only equation that gave predicted values that were not significantly different from measured VO_2max. The results, of the ACSM equation, found in this thesis correspond to the findings by Stanforth et al, that the ACSM equation (5^{th} edition) is a fairly valid estimate of aerobic capacity.

In the present investigation, the Latin and Berg revised ACSM equation was not found to provide valid results. This is in accordance with Stanforth et al. The Latin and Berg equations was evaluated in the anticipation of finding accurate results since the equation was developed for young women, similar to the age and fitness levels of the subjects in this study. The Latin and Berg equation resulted in estimates that were less accurate than the ACSM equations (underpredicted by 3 $ml \bullet kg^{-1} \bullet min^{-1}$), and therefore the equation was not used in the statistical analysis of this thesis.

The basis of the ACSM equation has been criticized for its use of age-predicted maximum heart rate for extrapolating the maximal exercise intensity (21). Whaley et al studied a large adult population and found that 5% of men and 7% of women have a maximum heart rate that is 15 beats/min (bpm) lower than age-predicted max heart rate, and 13% of men and 9% of women have a maximum heart rate that is 15 bpm higher (67). Griewe et al found that 10% of their subjects had maximum heart rates that were >15 bpm above age-predicted max heart rate and that 23% of their subjects had maximum heart rates that were >15 bpm below age-predicted maximum heart rate (21). Since most individuals do not exactly obtain their age-predicted maximum heart rate during exercise, the use of age-predicted maximum heart rate in the ACSM equation has

been blamed for the unreliability of estimates by up to 30% (21, 33, 34). Once correcting for actual maximum heart rates, Griewe et al found an improvement in VO_2max estimates from a 26% overprediction to 19.5% (21). This was because age-predicted heart rate significantly overestimated measured maximum heart rate in 2/3 of their subjects. However, in the present study, all of our subjects reached their maximum age-predicted heart rate values within ± 6 bpm which could be the reason we found the ACSM equation to provide a better estimate than previous research. In fact, when the measured maximal heart rate was input into the regression equation to estimate VO_2max, no significant difference was found between VO_2max estimates- comparing the values obtained from actual and age-predicted heart rates. However, the use of actual maximal heart rate decreased the mean VO_2max estimate, thus providing a more severe underprediction. Since an overestimation of age-predicted maximum heart rate leads to an overprediction of VO_2max and 2/3 of their subjects did not reach their age-predicted maximums, the use of actual maximal heart rate improved the VO_2max estimates in the Greiwe et al study (21). However, with high intraindividual variability in maximal heart rate (± 15 bpm) it is logical to think that there should be a uniform distribution of underestimations and overestimations of VO_2max within a given population. For example, in this thesis 41% of subjects had lower age-predicted maximum heart rates, while 50% of the subjects had higher age-predicted maximum heart rates (the other 9% reached heart rates that equaled their age predicted maximums). Therefore, the use of maximum age-predicted heart rate by the ACSM equation accounts for the individuals at both extremes allowing its use with any population. Also, the purpose of submaximal testing is to avoid the dangers and complications associated with a maximal test, which

would be necessary if actual maximal heart rate measurements were to be used in the ACSM submaximal equation. As seen in this thesis, the use of measured maximal heart rate does not improve the predictive ability of the ACSM equation.

Based on the results of this study, the prospective ACSM equation that will be published in the 6th edition of the *ACSM's Guidelines for Exercise Testing and Prescription*, provides a more accurate estimate of VO_2max than the original ACSM equation from the 5th edition of the ACSM Guidelines. The new ACSM equation estimated VO_2max values that were closer to the true max, than the original ACSM predicted values, by 0.17 and 0.24 $ml \bullet kg^{-1} \bullet min^{-1}$ in the Q-L and Q-F phases, respectively. Although a fairly reasonable estimate overall, the original ACSM cycle ergometry equation was found to underestimate VO_2 at lower workloads and overestimate VO_2 at higher workloads, which is the reason that a new ACSM equation was developed (29, 33, 34, 41). The same researchers that discovered this problem found a solution by increasing the intercept and decreasing the slope, however the new equations still did not provide valid estimates (29). The necessary revisions were made to the original ACSM equation using the data from Londeree et al and Latin and Berg, however specifically "measured" VO_2 from repeated measurements taken by Stuart et al was used to develop the prospective ACSM equation (29). The data from Stuart et al consisted of actual VO_2 measurements from subjects who exercised at a variety of workloads on a Monark cycle, where the cadence was kept constant and gases were consistently measured (29). Upon validation, the new ACSM equation estimated VO_2 at each submaximal workload within ± 0.07 l/min (29). Since the new equation takes into account the VO_2 at "rest" for the work of moving the legs even at zero load and the O_2

cost per watt of external load, the new ACSM equation clearly accounts for all three components of the metabolic equation with the addition of the horizontal component of zero load pedaling (29). This is in comparison to the 5th edition ACSM submaximal cycle ergometry equation that only accounted for the vertical (power output and tension, revolutions and pedal rate) and resting (body weight) components of the metabolic equation (43). The addition of these modifications has provided an improved equation for the estimation of VO_2max.

The AF test, based on the A-R nomogram, is a better predictor of maximal aerobic capacity in young women on oral contraceptives than the ACSM test. In both the Q-L and Q-F phases, the mean $\dot{V}O_2max$ estimates of the AF test were closer to the true maximal values than those from the ACSM test, regardless of which equation was used (Figure 5). Although individual estimated VO_2max values appear to be less accurate than the ACSM test (Figure 8), the AF test placed more subjects in the correct fitness category or higher, while the ACSM test placed the majority of the subjects in a lower fitness category than they should have been classified. Both tests are based on a linear heart rate-VO_2 relationship, however the AF and ACSM tests use different protocols and different equations for computing the estimated values. The ACSM cycle ergometry equation uses pedaling frequency, meters per pedal revolution, resistance applied to the ergometer and an estimate of resting metabolism to predict the oxygen cost of cycle ergometry (2). The testing protocol consists of four 3-minute stages where the subject works at progressively increasing submaximal workloads (in this study the subjects worked at 0.5, 1.5, 2.0, and 2.5 kp) achieving a steady-state heart rate at each stage prior to increasing the load. Maximal work intensity can then be estimated and used to

calculate the predicted VO_2max. The main variables in this equation include body weight and heart rate response. In contrast, the AF test uses the subject's heart rate response to a single predetermined submaximal workload over a 6-minute time period. A computer calculation, based on the A-R nomogram, computes the estimated VO_2max using age, sex, weight, height, average ending heart rate, a body surface conversion constant and the final workload. The AF calculation uses more variables than the ACSM equation, in estimating VO_2max. The test progresses based on the individual heart rate response of the subject, and the final equation uses variables specific to the subject. Therefore, based on the results of this study, taking more subject-specific variables into consideration during testing provides a more accurate estimate of VO_2max.

This study analyzed the relationship between the fitness level of the individual and the predictive ability of the 3 submaximal equations. Hartung et al reported that the validity of the AF test in aerobically fit and unfit men was consistent in its overpredictions and underpredictions relative to fitness level (25). Estimated values in highly fit subjects tended to overpredict while estimated values in less active individuals tended to underpredict (25). In the same type of study, using only women, Hartung et al found the same results between the fit and unfit subjects (24). Rowell et al found a higher degree of underestimation, with the A-R submaximal cycle ergometry test, in untrained individuals (26%) as compared to trained athletes (6%) (55). In contrast, the present study along with Siconolfi et al found no statistically significant relationship between fitness level and the predictive ability of the AF or ACSM tests (57). However, the present study used a homogeneous group of fairly active subjects with a small range of fitness levels (VO_2max ranging from 30 $ml \bullet kg^{-1} \bullet min^{-1}$ to 45 $ml \bullet kg^{-1} \bullet min^{-1}$) and

Siconolfi et al primarily used inactive subjects (57). Therefore, although fitness level did not contribute to differences in the predictive ability of the three equations in this study, it cannot be concluded that the equations are equally valid for all ranges of individual fitness.

Temperature

Our finding that the body temperature of female OC users is increased by approximately 0.3 °C in the Q-L phase of the menstrual cycle is in agreement with earlier studies (10, 22, 42, 54). Previous research has shown that this rise in temperature is mediated by the action of progesterone in normal menstruating women (8, 26, 27, 52) and that the opposite effect, a decrease in temperature occurs with the administration of estrogen (8, 62). According to Carpenter and Nunneley, in normal menstruating women, when progesterone concentrations are high in the luteal phase they seem to override the estrogen influence and cause this increase in temperature. However, during ovulation when progesterone levels are at their lowest, body temperature is decreased by the high estrogen (8). Tankersley et al also found that during estrogen replacement therapy body temperature was decreased (62). The observations in the present study agree with these previous reports of a significantly higher temperature in the Q-L phase (P=0.0001) independent of pill type. However, variations in this hormonal thermoregulatory control could exist between the different estrogen and progestin components of each pill formulation. In Figure 2, the average temperature curve for each of the pill groups, across one OC menstrual cycle is plotted. Group P4 had the highest mean temperature

over the 28-day cycle, while group P1 had the lowest temperatures. Group P1 had a significantly lower temperature than P4 (P=0.002) and P2 (P=0.007) in the Q-L phase (P3 was not significantly different). The significant differences in the temperature curves, between the pill types contained in groups P1 and P4, were further analyzed by comparing the pill formulations (refer to Table 4). Based on the ANOVA results there was no statistically significant difference between the estrogen content of the different pill types. However it is possible, since circulating estrogen concentrations were not measured, that the slightly higher ethinyl estradiol (ie estrogen) content used in P1 caused a slight decrease in the P1 temperature curve during the Q-L phase. It is also possible that the synthetic progestins used in P4 are more potent, than those used in the other three groups. The progestins in P4 could have a stronger influence on temperature regulation than the progestins used in the other pills. Just as certain women are more sensitive to the endogenous hormonal variations in a normal menstrual cycle, there is likely a large interindividual variability in response to the exogenous hormones contained in OC (35). It seems that synthetic progestins can raise body temperature, but the degree is dependent on the type of pill and the individual response to the synthetic hormones. As mentioned in previous studies, more research is needed on the thermoregulatory effects of the various progestins used in OC pills today.

Differences in Pill Type

Based on the results of this study, it can be concluded that the type of pill used by each subject was irrelevant to the results. There were no significant phase-related

differences in pill types between any of the tests or testing parameters studied, thus pill type did not influence any of the variables. The small differences in heart rate and VO_2max that are noted in the results section, can be attributed to the fitness levels of the individual subjects and not to pill type. Women in group P4 had the lowest heart rates, while those in group P2 had the highest heart rates across all four workloads of the ACSM test, in both phases. Group P2 was also the main contributor to the underprediction of values while P4, although not significant because of small group numbers (n=2), contributed to the overprediction seen in the AF test. This is because P2 contains most of the subjects with lower fitness levels (VO_2max approximately 35 $ml \bullet kg^{-1} \bullet min^{-1}$) especially when compared to P4 which contained the more fit individuals (VO_2max approximately 40 $ml \bullet kg^{-1} \bullet min^{-1}$). Subjects with lower VO_2max values would likely have higher exercising heart rates at submaximal intensities when compared to subjects with higher VO_2max values. The pill group and fitness level influence on the differences in heart rate disappeared when analyzing the difference in heart rates between the Q-L and Q-F phases for each pill group. Therefore, differing individual fitness levels and not pill type is most likely the reason for the apparent differences in heart rate and estimated VO_2max between pill groups.

Reliability Between the Q-L and Q-F Phase Measurements

Although the measured VO_2max was slightly higher in the Q-F phase, all of the estimated values were lower than the corresponding Q-L values, and significantly so for the AF test (AF P=0.02, ACSM P=0.07, new ACSM P=0.06). Since workload, age, sex

and body weight remained relatively constant between phases, heart rate was the only variable that could have caused the changes in VO_2max estimates between phases. A higher exercising heart rate will predict a lower VO_2max value when compared to a lower heart rate response at the same workload. Therefore, the tendency for a significantly greater underprediction in the Q-F phase must be due to the hormonally-influenced change in exercising heart rate responses to submaximal exercise.

Heart rate was significantly higher during the Q-F phase ($P<0.05$), when each test underpredicted VO_2max. Numerous studies have found no difference in heart rate during exercise across the two phases of the natural menstrual cycle (13, 15, 27, 28, 30, 37, 48). While some others have found a significant increase in heart rate during the luteal phase (26, 52, 56) which these authors attributed to changes in plasma volume or body core temperature. In normal menstruating women, Hessemer and Bruck found heart rates that were 6 bpm higher in the luteal phase (26). Pivarnik et al measured an increased heart rate of 10 bpm in the luteal phase of an ovulatory menstrual cycle also (52). Both of these authors postulated that the increased progesterone in the luteal phase, and subsequent increase in body temperature, has a negative influence on exercise performance because of the increase in heart rate response. These findings contributed to the original hypothesis of this thesis, which has since been proven wrong.

It is possible that the synthetic progestins in OC have a different influence on body temperature and heart rate as compared to the changes attributed to endogenous progesterone. However, studies with women on oral contraceptives are rather limited and offer conflicting results. Rogers and Baker found that women on OC had an elevated heart rate in the Q-L phase, compared to the Q-F phase, by approximately 6-7 beats/min

during submaximal exercise (54) and attributed the difference to the elevated body core temperature. Some studies have found no differences in submaximal or maximal exercising heart rate between the Q-F and Q-L phases (36, 42, 66). Only one other oral contraceptive study to date, consistent with the results reported here, has found higher heart rates during the Q-F phase (81 ± 12 vs. 96 ± 15 beats/min, $P<0.05$) however it was under resting, heat stress conditions and not during exercise (10). The present study found significantly higher Q-F heart rates during both the AF and ACSM testing protocols, which is the opposite of the original hypothesis of this study. Many of the previous studies may have used subjects who were on different OC than the subjects used in this thesis, with differing amounts of estrogens or progestins, or possibly even pills containing progestins only. However, this study has concluded that the type of pill used by each subject was irrelevant to the results. Yet all of our subjects were on low-dose combination pills, so the influences of a progestin-only pill or high-dose combination pills were not evaluated here. Thus, the diversity in both the estrogen and progestin components of oral contraceptives complicate the interpretations of OC studies and more research is needed in this field (35).

The next question to answer is why the heart rate response was higher in the Q-F phase. Since the only known variable between testing sessions was pill intake, it is logical to attribute the change in heart rate to the differing concentrations of synthetic hormones. Circulating hormonal concentrations were not measured here because the measurement of synthetic estrogen and progesterone are only possible using specialized HPLC procedures. Therefore, the following discussion has made certain assumptions about circulating synthetic hormone concentrations. Possible reasons for increased heart

rates in the Q-F phase include the direct influences of steroid hormones on heart rate or indirect changes in cardiovascular function due to changes in fluid volume.

The Estrogen Effect on Heart Rate and the CV Variables Influenced by Hormones

Hartard et al tested 6 women (mean 23 years) during submaximal cycle ergometry exercise for one normal menstrual cycle and then during another menstrual cycle while taking OC (23). They found that exercising heart rate was decreased from the luteal phase of the subject's normal menstrual cycle to the corresponding Q-L phase under OC use (23). According to these results, the female heart rate response to submaximal exercise seemed to decrease when a woman began using OC. Therefore, the observations in the present study may not necessarily indicate an increase in heart rate during the Q-F phase, but rather a decreased heart rate in the Q-L phase of OC use that is mediated by the synthetic hormones.

The few studies that have analyzed the effects of synthetic progestin or progesterone treatments on cardiovascular function reported unaltered heart rates during hormone administration to female ewes (51, 53). Hormone replacement therapy in postmenopausal women (both estrogen and progesterone together) increased cardiovascular variables such as cardiac output, blood volume and stroke volume, but did not change heart rate at rest (59). However, research aimed at the investigations of the female exercise response to the administration of these hormones is limited. Tankersley et al analyzed the influence of estrogen replacement therapy (1.25 mg of conjugated estrogens) on cardiovascular responses to submaximal exercise in the heat, and found that

body temperature and exercising heart rate were decreased (62). Although the amount of estrogen administered in the OC pill is smaller (0.04 mg compared to 1.25 mg) than the amount used by Tankersley et al, it is possible that the estrogen component of the pill, administered in the Q-L phase, caused a decrease in the heart rate response to submaximal exercise. The expected change in temperature seen with the administration of estrogen in the study by Tankersley et al was not seen in the present study. However, it is possible as previously mentioned, that this effect is masked by the progestin component which is known to have the dominant effect on temperature. Therefore the exogenous estrogen, through a different mechanism than temperature regulation, could be responsible for the decreased heart rate response during submaximal exercise in the Q-L phase. This interpretation would agree with the previously mentioned finding by Hartard et al that OC use causes a decrease in exercising heart rate during the Q-L phase when compared to the heart rate response to exercise in the luteal phase of the same subject's ovulatory menstrual cycle.

Several components of the cardiovascular (CV) system may be influenced by estrogen, therefore relating to a decreased heart rate in the Q-L phase. In normal menstruating women, estrogen has been shown to have a water-retaining effect because of its influence on the synthesis and release of antidiuretic hormone (19), leading to an increase plasma volume. Studies have shown that the effect on plasma volume is more pronounced with exogenously administered estrogens, especially in the presence of low blood progesterone concentrations (17). Since OC use inhibits the release of gonadotropins, consequently the circulating levels of endogenous progesterone and estrogen are very low. Bonen et al found the circulating progesterone concentration was

around 1.0 pmol/ml, during both the Q-F and Q-L phases (6). Therefore, the exogenous estrogen found in the OC pill along with the low blood progesterone concentration in the Q-L phase could cause a more pronounced effect on plasma volume. During exercise, Lehtovirta et al found an increase in blood volume, stroke volume and cardiac output in the Q-L phase for subjects using combination (progestin/estrogen) OC (38). It was suggested that the increased cardiac output was a result of the increased plasma volume, implying that there was an estrogen-dominant effect (36). Thus, it is possible that the estrogen component of the pill has an influence on plasma volume, causing plasma volume to increase during exercise. This would then cause an increased stroke volume, cardiac output and venous return resulting in a subsequent decrease in heart rate.

Several studies have shown that cardiac output is increased during submaximal exercise in women on combination estrogen and progestin OC (35, 38, 39, 66). Lehtovirta et al also found that blood volume and stroke volume increased during exercise in OC users (38) and Sites et al has demonstrated that hormone replacement therapy with progesterone and estrogen increases blood volume, cardiac output and stroke volume at rest (59). However, not one of these studies observed a difference in heart rate. Since humans are thought to lack the Bainbridge reflex, which states that there is no heart rate response to an increase in intrathoracic blood volume, it is not surprising that most authors did not find a difference (65).

An alternative interpretation for the phase-related difference in heart rate could be related to the secretion of endogenous hormones during the Q-F phase. Although the OC pill inhibits the secretion of gonadotropins in the Q-L phase, there is evidence that the

cessation of the pill during the Q-F phase causes a slight increase in follicle-stimulating hormone (FSH) (6). This increase in FSH can then stimulate the secretion of endogenous estradiol since there is no longer an inhibition mechanism in effect. This thesis examined subjects during the last 3 days of the Q-F phase, to ensure that testing occurred with the minimal possible influence of OC hormones still circulating in the blood stream. This left 4 days without ingestion of OC hormones, suggesting that there was enough time for the secretion of FSH and the subsequent secretion of estradiol. According to Grucza et al, higher heart rates during exercise are associated with an increased vasodilation in the follicular phase mediated by estrogen (22, 63). Therefore, our results would suggest that during submaximal exercise testing, the estrogen effect occurred from the increased circulating endogenous estradiol and low blood progesterone, plasma volume and cardiac output increased, and total peripheral resistance was decreased. This might account for the increased heart rates seen in the Q-F phase.

Conclusions

To date, there has not been a study that has examined the reliability and validity of a submaximal cycle ergometry test while controlling for the menstrual cycle or oral contraceptive use. This study found that overall, a heart rate-based submaximal cycle erogometry test is a valid predictor of maximal aerobic capacity in women on oral contraceptives in the Q-L phase. However, there were large individual deviations from the measured VO_2max values (within ± 20%), for both the AF and ACSM tests. There were very few individual estimated VO_2max values found within the ± 5% validity range.

However, the AF test placed more subjects in the correct fitness category, while the ACSM test placed the majority of subjects below their true VO_2max classification. In regard to reliability, neither the AF nor the ACSM tests were found to be very reliable between the Q-L and Q-F phases. During submaximal testing, alterations in heart rate occurred between the Q-F and Q-L phases via the influence of the synthetic hormones in the OC pill, thus altering the estimations of VO_2max. This occurred regardless of pill type and it was concluded that the different pill formulations used by subjects in this study did not cause different responses to exercise performance. Although the specific mechanistic influences of the OC hormones were not investigated, there was definitely evidence of performance alterations between the two phases that needs to be further analyzed.

Astrand and Rhyming reported that mechanical efficiency during testing can vary by as much as ±6% (4). Individual subjects who were not familiar with cycling may have been at a disadvantage due to poor mechanical efficiency, since heart rate is increased in order to meet the increased demand of oxygen transport. In our study it was possible that there was a learning bias, comparing the subject's second test to their first, however we controlled for this by randomizing the phase order of testing between subjects. It has been shown through both training and repetitive exposure to submaximal cycling however, that individuals can improve their mechanical efficiency (40, 61). Since the AF test was found to be a valid estimate of VO_2 max and the test is repeated each year for every member of the Air Force, mechanical efficiency should not be considered a major source of error. However, this conclusion can only be extended to individuals similar to the subject population in the present study of young, fairly active women on oral contraceptives. The use of homogeneous subjects could have caused the results of the AF

test to be within ± 5% of the measured value, as compared to other studies that used subjects of more diverse ages and fitness levels. Recall that the original Astrand-Rhyming equation was based on the data collected from healthy, active 18-30 year old men and women that are similar to the subjects used in this thesis.

Overall, the AF submaximal cycle ergometry test based on the A-R nomogram is a valid predictor of aerobic capacity in young women on oral contraceptives. However, this study has shown that it is a more reliable predictor of VO_2max when subjects are tested during the second week of the Q-L phase. The ACSM submaximal cycle ergometry test is also a valid predictor overall, but is not as accurate as the AF test in placing subjects in the appropriate fitness categories. The ACSM testing protocol should be used with the new ACSM equation for the most valid and reliable results, however this combination will provide a valid estimate in the Q-L phase only. The reliability between the Q-L and Q-F phases revealed a significantly higher underestimation of VO_2max in the Q-F phase, as compared to the estimated values in the Q-L phase, which is due to the significant difference between submaximal exercising heart rates in the two phases of OC use. The female heart rate response to submaximal exercise is influenced by the progestin and estrogen components of the OC pill. However, this synthetic hormonal influence may be attenuated by an unknown cellular mechanism outside the testing parameters studied in this thesis. Further research is needed to determine the precise influences of the different progestins and estrogens, as compared to endogenous hormones, and their effects on the exercising woman.

Also, future OC studies should look at the differences in exercise performance by testing women in the second week of pill taking (Q-L) and then during last 3 days of the

non-OC use phase (Q-F), using each subject as their own control. This would standardized the testing method and allow researchers to draw more concrete conclusions between OC studies.

Based on these results, the following recommendation can be made to the United States Air Force: 1) It is necessary that women are screened for OC use prior to the annual cycle ergometry test. 2) All women on OC should be tested during the second week of the Q-L phase, when results are both reliable and valid, allowing for standardized testing among annual tests. 3) Further testing should occur with a larger number of women on OC in the Air Force. Since the current thesis only accounted for a small percentage of the female AF population, it is necessary to measure the response of women in the AF using a wider range of ages and fitness levels.

REFERENCES

1. American College of Sports Medicine, *Guidelines for Exercise Testing and Prescription.* 4th Ed. Philadelphia: Lea & Febiger, 1991.

2. Andersen, R.E. and T.A. Wadden, Validation of a cycle ergometry equation for predicting steady-rate VO_2 in obese women. Medicine and Science in Sports and Exercise 27: 1457-1460, 1995.

3. Astrand, I., Aerobic work capacity in men and women with special reference to age. Acta. Physiol. Scand. 49 (Suppl. 169): 1-92, 1960.

4. Astrand, P.O. and I. Rhyming, A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during submaximal work. Journal of Applied Physiology 7: 218-221, 1954.

5. Berry, M.J., J.A. Storsteen, and C.M. Woodard, Effects of body mass on exercise efficiency and VO_2 during steady-state cycling. Medicine and Science in Sports and Exercise 25: 1031-1037, 1993.

6. Bonen, A., W. Haynes, and T.E. Graham, Substrate and hormonal responses to exercise in women using oral contrceptives. Journal of Applied Physiology 70: 437-444, 1991.

7. Borg, G.A.V., Psychophysical bases of perceived exertion. Medicine and Science in Sports and Exercise 14: 377-381, 1982.

8. Carpenter, A.J. and S.A. Nunneley, Endogenous hormones subtly alter women's response to heat sterss. Journal of Applied Physiology 65: 2313-2317, 1988.

9. Chang, R.T., G.P. Lambert, P.L. Moseley, F.K. Chapler, and C.V. Gisolfi, Effect of estrogen supplementationon exercise thermoregulation in premenopausal women. Journal of Applied Physiology 85: 2082-2088, 1998.

10. Charkoudian, N. and J.M. Johnson, Modification of active cutaneous vasodilation by oral contraceptive hormones. Journal of Applied Physiology 83: 2012-2018, 1997.

11. Daggett, A., B. Davies, and L. Boobis, Physiological and biochemical responses to exercise following oral contraceptive use [abstract]. Medicine and Science in Sports and Exercise 15: 174, 1983.

12. Davies, C.T.M., Limitations to the prediction of maximal oxygen intake from cardiac frequency measurements. Journal of Applied Physiology 24: 700-706, 1968.

13. DeSouza, M.J., M.S. Maguire, K.R. Rubin, and C.M. Maresh, Effects of menstrual phase and amenorrhea on exercise performance in runners. Medicine and Science in Sports and Exercise 22: 575-580, 1990.

14. Deuster, P.A., *E-mail correspondence regarding maximal treadmill versus maximal cycle ergometry as maximal comparison exercise in submaximal testing*, 1998.

15. Dombovy, M.L., H.W. Bonekat, T.J. Williams, and B.A. Staats, Exercise performance and ventilatory response in the menstrual cycle. Medicine and Science in Sports and Exercise 19: 111-117, 1987.

16. Fernhall, B. and W. Kohrt, The effect of training specificity on maximal and submaximal physiological responses to treadmill and cycle ergometry. Journal of Sports Medicine and Physiology 30: 268-275, 1990.

17. Fortney, S.M., W.S. Beckett, A.J. Carpenter, J. Davis, and H.Drew, Changes in plasma volume during bed rest: effects of the menstrual cycle and estrogen administration. Journal of Applied Physiology 65: 525-533, 1988.

18. Fox, E.L., A simple, accurate technique for predicting maximal aerobic power. Journal of Applied Physiology 35: 914-916, 1973.

19. Gaebelein, C.J. and L.C. Senay, Vascular volume dynamics during ergometer exercise at different menstrual phases. European Journal of Applied Physiology 50: 1-11, 1982.

20. Garlick, M.A. and E.M. Bernauer, Exercise during the menstrual cycle: variations in physiological baselines. Research Quarterly of the American Association for Health and Physical Education 39: 533-542, 1968.

21. Greiwe, J.S., L.A. Kaminsky, M.H. Whaley, and G.B. Dwyer, Evaluation of the ACSM submaximal ergometer test for estimating VO_2max. Medicine and Science in Sports and Exercise 27: 1315-1320, 1995.

22. Grucza, R., H. Pekkarinen, E.K. Titov, A. Kononoff, and O. Hanninen, Influence of the menstrual cycle and oral contraceptives on thermoregulatory responses to exercise in young women. European Journal of Applied Physiology 67: 279-285, 1993.

23. Hartard, M., P. Haber, L. Havelec, and D. Jeschke, Hemodynamics and ergometric performance modified by low dosage oral contraceptives. Zentralbl Gynakol 118: 37-41, 1996.

24. Hartung, G.H., R.J. Blancq, D.A. Lally, and L.P. Krock, Estimation of aerobic capacity from submaximal cycle ergometry in women. Medicine and Science in Sports and Exercise 27: 452-457, 1995.

25. Hartung, G.H., L.P. Krock, C.G. Crandall, R.U. Bisson, and L.G. Myhre, Prediction of maximal oxygen uptake from submaximal exercise testing in aerobically fit and nonfit men. Aviation , Space and Environmental Medicine 64: 735-740, 1993.

26. Hessemer, V. and K. Bruck, Influence of menstrual cycle on thermoregulatory, metabolic, and heart rate responses to exercise at night. Journal of Applied Physiology 59: 1911-1917, 1985.

27. Hirata, K., T. Nagasaka, A. Hirai, M. Hirashita, T. Takahata, and T. Nunomura, Effects of human menstrual cycle on thermoregulatory vasodilation during exercise. European Journal of Applied Physiology 54: 559-565, 1986.

28. Horvath, S.M. and B.L. Drinkwater, Thermoregulation and the menstrual cycle. Aviation, Space and Environmental Medicine 53: 790-794, 1982.

29. Howley, E., *Correspondence regarding the prospective ACSM equation*, 1999.

30. Jurkowski, J.E.H., N.L. Jones, C.J. Toews, and J.R. Sutton, Effects of menstrual cycle on blood lactate, O_2 delivery and performance during exercise. Journal of Applied Physiology 51: 1493-1499, 1981

31. Kenney, W.L., *Communication regarding the prospective ACSM equation*, 1999.

32. Krock, L.P., *Metabolic energy costs of USAF explosive ordinance disposal render safe procedures: field determinations*. Brooks AFB, TX: Air Force Systems Command, Crew Systems Directorate, 1991: Technical Report AL-TR-1991-0028.

33. Lang, P., R. Latin, K. Berg, and M. Mellion, The accuracy of the ACSM cycle ergometry equation. Medicine and Science in Sports and Exercise 24: 272-276, 1992.

34. Latin, R.W. and K.E. Berg, The accuracy of the ACSM and a new cycle ergometry equation for young women. Medicine and Science in Sports and Exercise 26: 642-646, 1994.

35. Lebrun, C.M., Effect of the different phases of the menstrual cycle and oral contraceptives on athletic performance. Sports Medicine 16: 400-430, 1993.

36. Lebrun, C.M., The effect of the phase of the menstrual cycle and the birth control pill on athletic performance. Clinics in Sports Medicine 13: 419-437, 1994.

37. Lebrun, C.M., D.C. McKenzie, J.C. Prior, and J.E. Taunton, Effects of menstrual cycle phase on athletic performance. Medicine and Science in Sports and Exercise 27: 437-444, 1995.

38. Lehtovirta, P., J. Kuikka, and T. Pyorala, Hemodynamic effects of oral contraceptives during exercise. International Journal of Gynaecology and Obstetrics 15: 35-37, 1977.

39. Littler, W.A., R. Bojorges-Bueno, and J. Banks, Cardiovascular dynamics in women during the menstrual cycle and oral contraceptive therapy. Thorax 29: 567-570, 1974.

40. Lockwood, P.A., J.E. Yoder, and P.A. Deuster, Comparison and cross-validation of cycle ergometry estimates of VO_2 max. Medicine and Science in Sports and Exercise 29: 1513-1520, 1997.

41. Londeree, B.R., J. Moffitt-Gerstenberger, J.A. Padfield, and D. Lottman, Oxygen consumption of cycle ergometry is nonlinearly related to power output and pedal rate. Medicine and Science in Sports and Exercise 29: 775-780, 1997.

42. Lynch, N.J. and M.A. Nimmo, Effects of menstrual cycle phase and oral contraceptives on intermittent exercise. European Journal of Applied Physiology 78: 565-572, 1998.

43. Mahler, D.A., V.F. Froelicher, N.H. Miller, and T.D. York, *ACSM's guidelines for exercise testing and prescription*. 5th Ed. Baltimore: Williams and Wilkins, 1995.

44. Margaria, R., P. Aghemo, and E. Rouelli, Indirect determination of maximal O_2 consumption in man. Journal of Applied Physiology 20: 1070-1073, 1965.

45. Maritz, J.S., J.P. Morrison, N.B. Styrdom, and C.H. Wyndham, A practical method of estimating an individual's maximal oxygen intake. Ergonomics 4: 97-122, 1961.

46. Myrhe, L.G., *Firefighter Physical Fitness Program*. Washington DC: Dept of the Air Force, 1989; Air Force Pamphlet 97.3.

47. Myrhe, L.G., *A submaximal cycle ergometry exercise protocol for predicting aerobic capacity from the Astrand-Rhyming nomogram: validation against measured values by indirect calorimetry*. Dept of Anatomy and Physiology, Indiana University; 1967 Human Performance Laboratory Methods.

48. Nicklas, B., A. Hackney, and R. Sharp, The menstrual cycle and exercise: performance, muscle glycogen and substrate responses. International Journal of Sports Medicine 10: 264-269, 1989.

49. Notelovitz, M., C. Zauner, L. Mckenzie, Y. Suggs, C. Fields, and C. Kitchens, The effect of low-dose contraceptives on cardiorespiratory function, coagulation, and lipids in exercising young women: a preliminary report. American Journal of Obstetrics and Gynecology 156: 591-598, 1987.

50. Patton, J.F., J.A. Vogel, and R.P. Mello, Evaluation of a maximal predictive cycle ergometry test of aerobic power. European Journal of Applied Physiology 49: 131-140, 1982.

51. Pecins-Thompson, M. and M. Keller-Wood, Effects of progesterone on blood pressure, plasma volume, and responses to hypotension. American Journal of Physiology 272: R377-85, 1997.

52. Pivarnik, J.M., C.J. Marichal, T. Spillman, and J. J.R. Morrow, Menstrual cycle phase affects temperature regulation during endurance exercise. Journal of Applied Physiology 72: 543-548, 1992.

53. Roesch, D.M. and M. Keller-Wood, Progesterone rapidly reduces arterial pressure in ewes. American Journal of Physiology 272: H386-91, 1997.

54. Rogers, S.M. and M.A. Baker, Thermoregulation during exercise in women who are taking oral contraceptives. European Journal of Applied Physiology 75: 34-38, 1997.

55. Rowell, L.B., H.L. Taylor, and Y. Wang, Limitations to prediction of maximal oxygen uptake. Journal of Applied Physiology 19: 919-927, 1964.

56. Schoene, R.B., H.T. Robertson, D.J. Pierson, and A.P. Peterson, Respiratory drives and exercise in menstrual cycles of athletic and nonathletic women. Journal of Applied Physiology 50: 1300-1305, 1981.

57. Siconolfi, S.F., E.M. Cullinane, R.A. Carleton, and P.D. Thompson, Assessing VO_2max in epidemologic studies: modification of the Astrand-Rhyming test. Medicine and Science in Sports and Exercise 14: 335-338, 1982.

58. Siconolfi, S.F., C.E. Garber, T.M. Lasater, and R.A. Carleton, A simple, valid step test for estimating maximal oxygen uptake in epidemiology studies. American Journal of Epidemiology 121: 382-390, 1985.

59. Sites, C.K., M.D. Tischler, J.A. Blackman, J. Niggel, J.T. Fairbank, M. O'Connell, and T. Ashikaga, Effect of short-term hormone replacement therapy on left ventricular mass and contractile function. Fertil Steril 71: 137-43, 1999.

60. Software, *Air Force Fitness Program, Fitness Assessment Software*, 1996, AFMC.

61. Stanforth, P.R., M.D. Ruthven, J. Gagon, C. Bouchard, A.S. Leon, D.C. Rao, J.S. Skinner, and J.H. Wilmore, Accuracy of prediction equations to estimate submaximal VO_2 during cycle ergometry: The HERITAGE Family Study. Medicine and Science in Sports and Exercise 31: 183-188, 1999.

62. Tankersley, C.G., W.C. Nicholas, D.R. Deaver, D. Mikita, and W.L. Kenney, Estrogen replacement in middle-aged women: thermoregulatory responses to exercise in the heat. Journal of Applied Physiology 73: 1238-1245, 1992.

63. Tarnopolsky, M., *Gender Differences in Metabolism*, Boca Raton: CRC Press, 1991.

64. Thomas, J.A. and E.J. Keenan, Principles of endocrine pharmacology. Plenum Medical, New York 179-187, 1986.

65. Vatner, S.F. and M. Zimpfer, Bainbridge reflex in conscious, unrestrained and tranquilized baboons. American Journal of Physiology 240: H164-7, 1981.

66. Walters, W.A.W. and Y.L. Lim, Cardiovascular dynamics in women receiving oral contraceptive therapy. Lancet 2: 879-881, 1969.

67. Whaley, M.H., L.A. Kaminsky, G.B. Dwyer, L.H. Getchell, and J.A. Norton, Predictors of over- and underachievement of age-predicted maximal heart rate. Medicine and Science in Sports and Exercise 24: 1173-1179, 1992.

69. Williford, H.N., K. Sport, and N. Wang, The prediction of fitness levels of USAF officers: validation of cycle ergometry. Military Medicine 159: 175-178, 1994

70. Yousef, M.K., C.T. Rasmussen, and L.G. Myrhe, *Physiological stresses associated with U.S. Air Force groundcrew activities*. 1988, USAF School of Aerospace Medicine: Brooks AFB, TX: Technical Report USAFSAM-TR-85-61.

71. Zwiren, L.D., P.S. Freedson, A. Ward, S. Wilke, and J.M. Rippe, Estimation of VO_2 max: A comparative study analysis of five exercise tests. Research Quarterly of Exercise and Sport 62: 73-78, 1991.

APPENDIX A

WOMEN'S HEALTH QUESTIONNAIRE

Noll Physiological Research Center
The Pennsylvania State University

Women's Health Questionnaire

Please check the appropriate answer:

O Yes	O No	Have you been using Oral Contraceptives for one year or more?
O Yes	O No	Do you have any chronic medical condition, for example: diabetes, pregnancy, or inflammatory bowel disease?
O Yes	O No	Do you have any minor injuries which will limit you from exercising on a treadmill or stationary bike?
O Yes	O No	Are you taking any other medications besides Oral Contraceptives? Please include pain relievers, aspirin, eye drops, creams, sleeping pills, etc.

Drug- How much- How often-

O Yes	O No	Do you smoke?
O Yes	O No	Are you currently following a special diet? If yes (specifiy):____________________
O Yes	O No	Do you exercise regularly? How many times per week?__________ At what intensity (1-5, with 1 being the lowest):____________

APPENDIX B

TEMPERATURE CHART

Name ________________

ID ____________________

Exercise																												
Day of Cycle	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99
	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98	98
	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97	97
	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Month/Year	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Day of Month																												

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Menstrual Chart																												

Menstrual Chart:

Normal Flow = N No Flow = Blank Light Flow = L Heavy Flow = H Pain = P

APPENDIX C

SUMMARY SHEET

PENNSTATE

1855

General Clinical Research Center

[illegible]
Fax [illegible]

The Pennsylvania State University
[illegible] Laboratory
University Park, PA [illegible]

SUMMARY SHEET

Date ______________________

Subject Name ______________________ Id. Number ______________________

Social Security Number ______________________

Address ______________________

____

Phone Number - Home ______________________

Work ______________________

DOB ______________________ Age ______________________

Height ______________________ Weight ______________________

Allergies ______________________

Physician ______________________

Address ______________________

____

Phone Number ______________________

APPENDIX D

INFORMED CONSENT

INFORMED CONSENT FORM
The Pennsylvania State University

Title of Project: Submaximal Cycle Ergometry as a Predictor of Maximal Aerobic Capacity in Women on Oral Contraceptives

Investigators: Jannell C. Zicarelli, 2nd Lt, USAF; Brittney Salkeld; Joseph Cannon, PhD

This is to certify that I, ______________________________, have been given the following information regarding my participation as a volunteer in a program of investigation under the supervision of Jannell Zicarelli, Brittney Salkeld and Dr. J.G. Cannon. I am 18 years of age or older and/or a full-time student of the Pennsylvania State University.

1. **Purpose of the study**
   This investigation is intended to study the reliability and validity of submaximal cycle ergometry tests for women on oral contraceptives. Submaximal tests provide an estimate of, maximal aerobic capacity (VO_2 max) however results vary in reliability and validity. Certain factors, such as the menstrual cycle and oral contraceptives, are not accounted for during submaximal testing. It is possible that women using oral contraceptives have elevated exercising heart rates and submaximal cycle ergometry tests are based on heart rate response to exercise. Therefore, testing needs to be conducted, using approximately 12 women, to determine the reliability and validity of submaximal testing for women on oral contraceptives.

2. **Procedures to be followed**
   I have been selected as a healthy young woman using oral contraceptives. I will fill out a questionnaire which will determine my oral contraceptive use, menstrual cycle history, exercise history and medication.

   Once I am selected as a subject in this study, I will document my body temperature for one entire menstrual cycle, according to the instructions given to me by the principal investigators, Jannell Zicarelli and Brittney Salkeld. I will use the digital thermometer I was given and return it when I have finished the 28 day cycle.

   I understand I am to report to Noll Laboratory for testing on a minimum of 4 scheduled dates. The first will be for maximal testing followed two days later, by two submaximal tests. This will occur during two phases of my menstrual cycle. Once on days 0-7 and the second visit will occur during days 14-21.

   When I am instructed to come in for testing, I will report to Noll Laboratory between 9 am and 12 noon. I understand a blood and urine

sample will be taken prior to submaximal exercise in both phases of the cycle, thus I will have samples taken twice. This is for the measurement of progesterone levels in my blood and urine.

Prior to submaximal testing sessions, I will be asked to complete the MFI-20 (Multidimensional Fatigue Inventory). This will be used to assess various self-reported aspects of fatigue. It consists of 20 statements to which I must respond.

Throughout the submaximal testing sessions I will be asked to rate my own perception of overall effort every minute using the Borg Scale of Ratings of Perceived Exertion.

3. **Discomforts and Risks**

   There is the discomfort of a needle prick and the risk of bruising during the procedure of drawing blood. However, since blood will only be taken twice, the risk is very minimal. Each blood sample will be approximately 2 tsp or 10 cc. Since a maximal test requires the subject to exercise to exhaustion, there is a risk of overexertion and faintness. I understand that I will be exercised to fatigue and that breathlessness, chest pain, and/or any other symptoms indicate to the medical personnel and myself that I should stop exercise.

4. **Potential benefits**

   The results of this study will provide information about the reliability and validity of submaximal cycle ergometry tests in women on oral contraceptives. Since many organizations, including the United States Air Force, use this type of testing to assess the fitness levels of individual members, results could alter existing policies and procedures in regards to women and fitness assessment. As for myself, I will receive information about my own physical fitness level and how to improve my maximal aerobic capacity for healthier living. Maximal aerobic capacity is a measure of the body's ability to transport oxygen to tissues in strenuous activity. In understanding this value, I will be able to assess my own cardiovascular fitness. I will also be compensated in the sum of $50, with $10 given each visit for testing and $10 given at the completion of the study.

5. **Time duration of the procedures and study**

   I understand that I will be required to note my body temperature throughout the month prior to testing (i.e. one menstrual cycle). I also understand that testing will occur during the months of January and February 1999. I will be required to report to Noll Laboratory at the specified times and complete 6 tests, as arranged and instructed by the principal investigator.

6. **Statement of confidentiality**
I understand that my participation in this research is confidential. Only the investigator and her assistants will have access to my identity and to information that can be associated with my identity. In the event of publication of this research, no personally identifying information will be disclosed.

7. **Right to ask questions**
I understand that I can contact the principal investigators at any time, with questions related to the research, at the following number: H 235-5739 and W 865-0368. I have been given an opportunity to ask any questions I may have, and all such questions or inquiries have been answered to my satisfaction.

8. **Compensation**
I understand that medical care is available in the event of an injury resulting from research but that neither financial compensation nor free medical treatment is provided. I also understand that I am not waiving any rights that I may have against the University, for injury resulting from negligence of the University or investigators.

9. **Voluntary participation**
I understand that my participation in this study is voluntary, and that I may withdraw from this study at any time by notifying the investigator. My withdrawal from this study or my refusal to participate will in no way affect my care or access to medical services.

This is to certify that I consent to and give permission for my participation as a volunteer in this program of investigation. I understand that I will receive a signed copy of this consent form. I have read this form, and understand the content of this consent form.

______________________________ _______________

Subject's Signature Date

I, undersigned, have defined and fully explained the studies involved to the above volunteer.

______________________________ _______________

Investigator's Signature Date